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StudyPRN

Endocrinology & Diabetes SCE 2021

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Question 1

A 55 year old male is admitted with abdominal pain and vomiting under the surgical team. A CT scan is arranged. Gallstones are noted but note is also made of a 3cm left adrenal adenoma. The surgeons plan a cholecystectomy but want advice regarding the adrenal lesion. On examination, the patient is well, temperature is normal and the pulse is 80 bpm with a blood pressure of 124/70 mmHg. Routine biochemistry is reported as normal.
Which of the following would be the most appropriate investigation for this patient?

- **A)** 24hr urine collection for catecholamines
- **B)** 24hr urine collection for urine free cortisol
- **C)** MRI adrenals
- **D)** No further investigation required
- **E)** Plasma renin:aldosterone activity

Answer

Correct answer : 24hr urine collection for catecholamines

This patient has been admitted with abdominal pain and CT has revealed what at first sight appears to be an incidentaloma. These occur in up to 10% of the population with imaging yet it is important to investigate thoroughly. The most important thing to exclude, particularly in view of any further intervention, is a phaeochromocytoma as catastrophic consequences can ensue following anaesthesia or surgical intervention. There is little added benefit of MRI over CT in the examination of the adrenals and in this case would not exclude phaeochromocytoma.

Reference:

Investigation of adrenal adenoma

Question 2

A 45 year old male is referred for investigation of difficult to treat hypertension. He has a 6 year history of hypertension and takes amlodipine, ramipril and bendrofluazide yet his GP reports that he has a blood pressure consistently between 150-170 mmHg systolic.

On examination, he is obese with a BMI of 33.5 kg/m^2, his blood pressure is 160/84 mmHg and no other abnormalities are noted. His biochemistry reveals:

		Normal Ranges
Sodium	142 mmol/l	(134-144)
Potassium	3.4 mmol/l	(3.5 - 5.5)
Urea	5.5 mmol/l	(3-8)
Creatinine	100 micromol/l	(50-100)

Which of the following is the most appropriate management plan for this patient?

- **A)** Arrange MIBG scan
- **B)** Arrange MRI abdomen
- **C)** Check 24 hr urine catecholamines
- **D)** Check Plasma renin activity - aldosterone ratio (PRA:Aldo) on current therapy
- **E)** Stop bendrofluazide and check PRA:Aldo

Answer

Correct answer : Check Plasma renin activity - aldosterone ratio (PRA:Aldo) on current therapy

The resistant hypertension and the hypokalaemia suggest primary hyperaldosteronism - Conn’s syndrome. Although ACE inhibitors are associated with false negative test results, in clinical practice the PRA:Aldo ratio can be assessed without stopping these agents. In fact, ACEi may actually improve the sensitivity of the test. The only drugs to avoid for the initial screening for Conn's syndrome would be beta blockers (for 2 weeks) and spironolactone (for 6 weeks). Patients may require a subsequent confirmatory test if the initial PRA:Aldo ratio is suggestive of Conn's syndrome (typically above 1000). Confirmatory testing may for instance entail selective adrenal sampling.

Question 3

A 45 year old male has been noted to have a 5.2 cm adrenal adenoma after having MRI scan of the abdomen performed privately due to lower back pain. He was referred to endocrinology and urine free cortisol, urine catecholamines and plasma renin activity: aldosterone ratios were all normal.

What is the most appropriate action for this patient?

- **A)** Arrange repeat MRI in 1 year
- **B)** Arrange repeat MRI in 3 months
- **C)** Arrange repeat MRI in 6 months
- **D)** Reassure and discharge
- **E)** Refer for surgical removal

Answer

Correct answer : Refer for surgical removal

Although the investigations would suggest that this patient does not have a functional adenoma, one must be aware of the possible risk of carcinoma of the adrenals. The criteria for surgical removal of an adrenal tumour is a diameter of 4cm or more as the risk of primary carcinoma with such size is of the order of 1 in 30.

Question 4

A 42 year old female is co-incidentally noted to have a right 2cm adrenal lesion after having an MRI scan for possible colonic neoplasm. She is a known patient with type 2 diabetes with poor glycaemic control. On examination she has a BMI of 32 kg/m^2, a blood pressure of 146/88 mmHg and no abnormalities are otherwise noted. Her investigations reveal:

		Normal Ranges
24hr Urine free cortisol	230 nmol/d	(<280)
Urine catecholamines	normal	
9am Cortisol post 1mg overnight dexamethasone	88 nmol/l	(<50)
low dose dexamethasone suppression test	cortisol 110 nmol/l	
ACTH	10 pmol/l	(20 - 52)
Renin activity/Aldosterone ratio	450	(<800)
Midnight Salivary Cortisol	3 pmol/l	(Normal)

Which of the following is the most appropriate management for this patient?

- **A)** Arrange PET scan
- **B)** Discharge as this is an incidentaloma
- **C)** Refer to surgery for removal of lesion
- **D)** Repeat MRI of adrenals in 1 year
- **E)** Repeat MRI of adrenals in 6 months

Answer

Correct answer : Refer to surgery for removal of lesion

This patient appears to have non-suppressible cortisol on overnight dexamethasone testing and has a low ACTH concentration, yet UFC is normal. This is quite typical of subclinical Cushing's syndrome and with evidence of functionality, surgery would be recommended. With the increasing use of imaging, lesions of the adrenal glands occur in up to 10% of such scans and of these 10% may be subclinically functional.

AACE guidelines: management of adrenal incidentalomas

Question 5

A 22 year old male is diagnosed with an extra-adrenal phaeochromocytoma. There is no family history of note and there are no abnormalities to note on examination.
Which of the following genetic tests is likely to be most relevant in this patient?

- **A)** BRAC
- **B)** FGF 1
- **C)** NF type 1
- **D)** NF type 2
- **E)** SDH type B/D

Answer

Correct answer : SDH type B/D

Phaeochromocytoma susceptibility genes include Succinate dehydrogenase types B/D, VHL and RET proto-oncogene (MEN II). The phenotypic characteristics are likely to be present for NF 1 and so this is not the most appropriate investigation in this patient as well as the fact that this is an extra-adrenal phaeo. All patients with a phaeo diagnosed before 45 years of age should be investigated further for a potential genetic cause. Thus, the most appropriate answer here is screening for SDH mutations.

Question 6

A 53-year-old female is noted to have a 2 cm right adrenal incidentaloma whilst having an abdominal CT scan by the general surgeons. It has got benign features. Patient does not have features of endocrinopathy. Further investigation reveals the following results:

		Normal Ranges
U+Es	Normal	
Urine Catecholamines	Normal	
24hr Urine free cortisol	228 nmol/d	(<250)
plasma renin activity/aldosterone	480	(<850)
Cortisol post 1 mg overnight dexamethasone	38 nmol/l	

What is the most appropriate management for this patient?

- **A)** Arrange fine-needle aspiration (FNA) of adrenal
- **B)** Arrange PET scan
- **C)** Refer for adrenal surgery
- **D)** Repeat MRI scan in 3-6 months
- **E)** Reassure and discharge

Answer

Correct answer : Reassure and discharge

From investigations this mass is measured at 2 cm in diameter and has benign features. There is no evidence of functionality of this tumour from testing either. Therefore this patient can be reassured and discharged.

Reference:

Guidelines for the management of adrenal incidentalomas

https://eje.bioscientifica.com/view/journals/eje/175/2/G1.xml

Question 7

A 44 year old female is investigated for hypertension, central obesity, weight gain and proximal muscle weakness. Her investigations, including a low dose dexamethasone suppression test, confirm the clinical suspicion of Cushing's syndrome. These are the further investigations for this patient:

		Normal Ranges
Urine free cortisol	1020 nmol/d	(<250)
ACTH	<10 pmol/l	(20 - 50)
MRI adrenals	Bilateral nodular adrenal enlargement	
Pituitary MRI	Normal	

Which of the following is the most appropriate for this patient?

- **A)** Refer for bilateral adrenalectomy
- **B)** Refer for pituitary exploration
- **C)** Refer for inferior petrosal sinus sampling
- **D)** Treat with metyrapone
- **E)** Treat with mitotane

Answer

Correct answer : Refer for bilateral adrenalectomy

This patient has Cushing’s syndrome due to bilateral adrenal nodular enlargement which is independent of ACTH. This could be due to food-induced Cushing's and a meal test may be appropriate but the condition of ACTH-independent macronodular adrenal hyperplasia is described and seems the more probable explanation. The most appropriate treatment would be bilateral adrenalectomy.

Question 8

A 55 year old female is confirmed to have adrenal dependent Cushing's syndrome following presentation with a 6 month history of weight gain, weakness and thinning of the skin. CT of the abdomen has demonstrated a 9 cm left adrenal tumour and no other abnormalities are noted on this scan. An adrenalectomy is performed and histology reports an adrenal carcinoma.

Postoperative assessment reveals that the patient is steroid dependent and is prescribed 10 mg of hydrocortisone bd. She then undergoes a 1 mg overnight dexamethasone test and her 9am cortisol is measured at 22 nmol/l (150-800).

Which adjuvant therapy would most likely prolong the period of remission post radical surgery?

- **A)** Cisplatin
- **B)** Ketoconazole
- **C)** Metyrapone
- **D)** Mitotane
- **E)** No therapy required

Answer

Correct answer : Mitotane

This patient has an adrenal carcinoma which is the cause of Cushing's syndrome. Surgery has effectively treated the hypercortisolism and the patient now requires steroid replacement. Although at this stage the patient has no evidence of metastases, further serial scanning will be required. The prognosis associated with adrenal carcinoma is usually very poor although there is emerging evidence that the prognosis may be improved with adjuvant mitotane therapy.

Question 9

An 18 year old female who presents with oligomenorrhoea is found to have non-classical congenital adrenal hyperplasia (CAH). She enquires as to the risk of any of her future children suffering the disorder. Which of the following is correct concerning this risk?

- **A)** Virtually 0%
- **B)** 1%
- **C)** 5%
- **D)** 25%
- **E)** 50%

Answer

Correct answer : 1%

The patient has non-classical CAH which is most likely due to 21 hydroxylase deficiency. It is an autosomal recessive condition and the gene frequency is approximately 1 in 40 in the general population. Thus, the chances of this girl meeting a partner heterozygous for CAH is 1 in 40 yet she is homozygous for the condition. Therefore, the chances of her having a child with CAH is 1 in 2 with this person (50% chance that any children will be HMZ and 50% chance that they will be unaffected HTZ). Thus the overall chance of having a child with CAH would be 1 in 40 x 1 in 2 = 1 in 80 or roughly 1%.

Question 10

A 40-year-old man was referred to the endocrine clinic for his resistant hypertension. He is currently taking atenolol 50 mg od, bendrofluazide 2.5 mg od, doxazosin 4 mg od, amlodipine 10 mg od and ramipril 10 mg od.
On examination, his pulse was 64 beats per minute, his blood pressure was 162/96 mmHg, heart sounds were normal and there were no cushingoid features.
Investigations

		Normal Ranges
Serum Urea	4.4mmol/L	(2.5-7.5)
Serum Creatinine	88 µmol/L	(60-110)
Serum Potassium	3.06 mmol/L	(3.5–4.9)

Which is the most important medication to be discontinued before testing his aldosterone:plasma renin activity ratio?

- **A)** Amlodipine
- **B)** Atenolol
- **C)** Bendrofluazide
- **D)** Doxazosin
- **E)** Ramipril

Answer

Correct answer : Atenolol

Beta blockers are well recognised to cause a decrease in renin concentrations and hence could create a false positive result in a patient suspected of having Conn's syndrome. Consequently the drug should be stopped at least 2 weeks before testing the patient. Spironolactone would also need to be stopped prior to testing PRA/aldosterone ratios as this would result in falsely elevated aldosterone concentrations and should be stopped at least 6 weeks pre-testing. Although one might think that ACEis are associated with inaccurate results, this is not the case in primary hyperaldosteronism.

http://www.ncbi.nlm.nih.gov/pubmed/17315030

Question 11

A 22 year old woman was referred to clinic by her GP due to tiredness. She was not taking any medications. On examination, her blood pressure was measured at 180/98 mmHg.
Investigations by the GP revealed:

		Normal Ranges
Serum Sodium	140 mmol/l	(134 - 144)
Serum Potassium	3.2 mmol/l	(3.5 - 5)
Serum Urea	7.0 mmol/l	(3 - 8)
Serum Creatinine	92 µmol/l	(50-100)

Further investigations reveal:

		Normal Ranges
Plasma Renin Activity	5.2 pmol/ml/h	(1.1-2.7)
Serum Aldosterone	900 pmol/L	(135 -400)

Which of the following is the correct diagnosis?

- **A)** Bartter's Syndrome
- **B)** Conn's Syndrome
- **C)** Essential hypertension
- **D)** Fibromuscular dysplasia
- **E)** Gitelman's syndrome

Answer

Correct answer : Fibromuscular dysplasia

This young woman has hyperreninaemic hyperaldosteronism, hypertension and hypokalaemia. Due to her age, of the options listed, the most likely cause is fibromuscular dysplasia. The high renin concentration is a consequence of the relative renal ischaemia due to the fibromuscular dysplasia. This is not Bartter's syndrome as the patient is hypertensive. Gitelman’s similarly causes a low potassium concentration but with normal blood pressure. Conn's is associated with elevated aldosterone and low renin. This is unlikely to be essential hypertension as the renin would be expected to be normal as would aldosterone.

Question 12

A 33 year old male presents with lethargy and easy fatigue. He does not take any medication, has generally been well and denies the use of illicit drugs.

On examination, his BMI is 33.2 kg/m^2 his blood pressure is 118/72 mmHg and no abnormalities are otherwise noted. Investigations reveal:

		Normal Ranges
Sodium	142 mmol/L	(135-145)
Potassium	2.8 mmol/L	(3.5-5)
Urea	5.8 mmol/L	(3-8)
Creatinine	88 µmol/L	(50-100)

Which of the following is the most likely diagnosis?

- **A)** Apparent mineralocorticoid excess
- **B)** Bartter's syndrome
- **C)** Conn's syndrome
- **D)** Gitelman syndrome
- **E)** Hypokalemic periodic paralysis

Answer

Correct answer : Gitelman syndrome

The hypokalemia with normal blood pressure in a middle aged male without any skeletal abnormalities or retardation would suggest a diagnosis of Gitelman syndrome rather than Barrter’s syndrome.

Question 13

A 33 year old female presents with a three month history of fatigue, weight loss and is noted to have buccal and palmar crease pigmentation. Which of the following antibodies would be the most appropriate to check in this patient?

- **A)** Anti-21-hydroxylase antibody
- **B)** Anti-intrinsic factor antibody
- **C)** Anti-peroxidase antibody
- **D)** Anti-rho antibody
- **E)** Anti-TTG antibody

Answer

Correct answer : Anti-21-hydroxylase antibody

The suggested diagnosis here is Addison's disease with fatigue, weight loss and palmar/buccal pigmentation. Addison's disease is an autoimmune adrenalitis and anti-21 hydroxylase antibodies are noted in roughly 70-80% of patients.

Question 14

A patient with severe Cushing's disease is being pre-treated with metyrapone prior to elective surgical intervention. Upon which of the following enzymes does metyrapone act?

- **A)** 3 ß HSD
- **B)** 11 ß HSD
- **C)** 11ß hydroxylase
- **D)** 17 ß hydroxylase
- **E)** 21 ß hydroxylase

Answer

Correct answer : 11ß hydroxylase

Metyrapone is a competitive inhibitor of 11 ß hydroxylase enzyme (CYP11B1) which is expressed in the zona fasciculata and zona glomerulosa. This enzyme is required for conversion of deoxycortisol to cortisol and its inhibition leads to a decrease in cortisol concentration and an increase in ACTH through a feedback mechanism. Metyrapone is usually used during the preoperative management of patients awaiting surgery or if surgical treatment is contraindicated as a palliative measure. Nausea, hypertension and features of hirsutism are the major associated side effects. The dose titration of the drug is usually based on the cortisol day curve. In children ketoconazole is preferred over metyrapone as a preoperative medication (while awaiting adrenal surgery).

Question 15

A 32 year old female presents with hypokalaemia and metabolic alkalosis. She has a blood pressure of 124/76 mmHg. Her biochemistry shows:

		Normal Ranges
Sodium	135 mmol/L	(135-145)
Potassium	3.2 mmol/L	(3.5-5.5)
Mg	0.4 mmol/L	(0.7-1.0)
HCO3	28 mmol/L	(18-23)
Plasma renin activity	5.5 nmol/L	(0.5-2.2)
Aldosterone	722 pmol/L	(100-500)

What is the likely underlying diagnosis?

- **A)** Bartter's syndrome
- **B)** Congenital adrenal hyperplasia
- **C)** Conn's syndrome
- **D)** Gitelman's syndrome
- **E)** Liddle's syndrome

Answer

Correct answer : Gitelman's syndrome

Gitelman's syndrome is characterised by mutation in the SCL12A3 gene that encodes for a Na-Cl transporter at the distal convoluted tubule. As a result the affected individuals develop Na loss (salt wasting), hypovolemia, hypocalciuria, hypomagnesaemia and metabolic alkalosis. The fluid loss prompts activation of the renin-angiotensin system leading to an increase in both renin and aldosterone levels. The main differential diagnosis for Gitelman's syndrome includes Bartter's syndrome which usually affects children (rarely young adolescents). In contrast to Gitelman's syndrome the primary defect in Bartter's syndrome is at the Na-K-Cl transporter in the ascending limb of the loop of Henle, hypomagnesaemia is absent and patients usually have hypercalciuria.

Question 16

An 18 year old boy presents with hypertension which is controlled with a small dose dexamethasone 0.25mg daily. What's the likely inheritance of his underlying condition?

- **A)** Autosomal dominant
- **B)** Autosomal recessive
- **C)** Polygenetic
- **D)** X linked dominant
- **E)** X linked recessive

Answer

Correct answer : Autosomal dominant

Glucocorticoid remediable hypertension is a rare autosomal dominant condition due to gene duplication resulting in fusion of the 11 beta-hydroxylase gene to the aldosterone synthase gene. The resultant chimeric gene on activation leads to increased ACTH dependent aldosterone synthesis. The patients usually present with features of aldosterone excess (hypertension, hypokalaemia and metabolic alkalosis) with suppressed renin levels. The hypertension is exquisitely responsive to steroid therapy. The disease usually runs in families and clinical suspicion should be raised if a primary aldosterone excess is seen in more than one family members. The diagnosis of this condition is based on measurement of 18-oxocortisol and 18-hydroxycortisol levels and confirmed by genetic testing.

Question 17

A 45 year old woman undergoes investigation for her hypertension. She is noted to have a blood pressure of 170/100 mmHg associated with a potassium of 3.1 mmol/l (3.5-5). Review of the history reveals she takes no medication but likes eating liquorice. What is the likely underlying mechanism of her hypertension?

- **A)** Apparent mineralocorticoid excess
- **B)** Atypical variant of CAH
- **C)** Conn's syndrome
- **D)** Glucocorticoid remedial aldosteronism
- **E)** Pseudohypoaldosteronism

Answer

Correct answer : Apparent mineralocorticoid excess

Liquorice which is used in candies, cough mixtures and chewing tobacco contains glycyrrhetinic acid which inhibits the 11 beta-hydroxysteroid dehydrogenase (beta-HSD) enzyme. As a result the conversion of cortisol to the inactive cortisone (which is a more potent mineralocorticoid as compared to cortisone) is impaired at the level of the aldosterone receptor. This leads to a state of apparent mineralocorticoid excess, similar to the one seen with a genetic defect in 11beta-HSD enzyme. The patient's eating of liquorice can result in hypertension, hypokalaemia and metabolic alkalosis. The diagnosis can be confirmed by the measurement of urinary tetrahydrocortisol to cortisone ratio (increased levels of tetrahydrocortisol as compared to cortisone).

Question 18

A 70 year old male is investigated for a co-incidentally noted right adrenal adenoma which is undertaken an investigation of iron deficiency. The patient is referred to endocrinology and undergoes investigations which reveal that the adenoma is a functional cortisol secreting tumour and surgical excision is planned by the endocrine surgeons. Which of the following concerning peri and post operative management of this patient is important?

- **A)** Assessment of cortisol levels postoperatively and hydrocortisone to be given only if cortisol levels are low
- **B)** Low dose dexamethasone test post-operatively
- **C)** Fludrocortisone post operatively
- **D)** Measurement of morning postoperative cortisol
- **E)** Peri and postoperative hydrocortisone with further assessment of postoperative cortisol secretion

Answer

Correct answer : Peri and postoperative hydrocortisone with further assessment of postoperative cortisol secretion

The perioperative management of a cortisol producing adenoma includes glucocorticoid cover (generally hydrocortisone 100 mg IM/IV 6 hourly) until the patient is eating and drinking normally in the postoperative period. The dose of steroid cover is gradually tapered to a maintenance dose (prednisolone or hydrocortisone). As the contralateral adrenal gland may be suppressed due to long term excess cortisol production by the functional adrenal adenoma, reassessment of cortisol secretion is required and usually first performed at a 2 week postoperative interval. It may require months or even years for the contralateral adrenal gland to recover its function. Therefore the steroid cover may need to be continued.

Question 19

An Asian man is admitted with a history of weight loss, lethargy, nausea and vomiting. On examination he looks dehydrated and pigmented. His biochemical profile is as shown below:

		Normal Ranges
Sodium	124 mmol/L	(135-145)
Potassium	5.6 mmol/L	(3.5-5.5)
Urea	30 mmol/l	(7-20)
Creatinine	104 µmol/L	(60-115)
9 am cortisol	55 nmol/L	
30 min cortisol	220 nmol/L	(Post ACTH injection)

A CT image shows the presence of calcification within the adrenal gland. What is the likely aetiology of his adrenal insufficiency?

- **A)** Adreno leukodystrophy
- **B)** Adrenal tuberculosis
- **C)** Histoplasmosis
- **D)** Metastatic disease
- **E)** Sarcoidosis

Answer

Correct answer : Adrenal tuberculosis

Adrenal tuberculosis remains one of the commonest causes of adrenal insufficiency in the developing world with about 5% of the patients with disseminated tuberculosis (Miliary Koch's) developing significant adrenal insufficiency. A low threshold of suspicion to seek adrenal insufficiency is warranted in patients with tuberculosis as the symptoms and signs are nonspecific and at times are attributed to the underlying condition (tuberculosis). Adrenal tuberculosis is reversible with anti-tuberculosis medications if these are given at an early stage of the disease.

Question 20

A 49 year old male presents with abdominal pain and swelling. Following investigation, he is found to have metastatic adrenal carcinoma. Which of the following is likely to improve the prognosis in a patient with adrenal carcinoma?

- **A)** Aminoglutethimide
- **B)** Ketoconazole
- **C)** Metyrapone
- **D)** Mitotane
- **E)** Sunitinib

Answer

Correct answer : Mitotane

Mitotane is an adrenolytic drug which inhibits several enzymes involved in steroid/ mineralocorticoid synthesis including side chain cleavage, 11 beta-hydroxylase and 3 beta-hydroxy-steroid hydrogenase (3b-HSD). It is licensed for symptomatic treatment of advanced or inoperable adrenocortical carcinoma. The limitations with Mitotane therapy include delayed response and frequent side effects such as severe nausea, vomiting, hypogonadism and neurotoxicity.

Adjuvant Mitotane Chemotherapy for adrenal carcinoma NEJM 2007

Question 21

A 29 year old woman presents with hypertension and palpitations and is diagnosed with a paraganglioma. With which of the following mutations are paragangliomas associated?

- **A)** 21-Hydroxylase deficiency
- **B)** Loss of function of MAX mutation
- **C)** MENIN mutation
- **D)** HRPT 2 mutation
- **E)** VHL mutation

Answer

Correct answer : VHL mutation

The 2004 WHO classification of endocrine tumours classifies catecholamine secreting tumours into intra-adrenal paragangliomas (classically known as phaeochromocytomas) and extra-adrenal paragangliomas. The latter are further subdivided into those arising from sympathetic tissue or parasympathetic tissues (usually located in the head and neck, that rarely produce catecholamine). Hereditary catecholamine producing intra or extra- adrenal paragangliomas can be caused by one of the following germ line mutations:

1. RET proto-oncogene
2. von Hippel-Lindau gene (vHL)
3. Neurofibromatosis Type 1 gene (NF-1)
4. Succinate dehydrogenase subunit B (SDHB)
5. Succinate dehydrogenase subunit D (SDHB)

Patients with SDHB or SDHD are more likely to present with extra-adrenal disease, bilateral tumours and metastatic disease. According to the guidelines issued by The First International Symposium on Phaeochromocytomas (October 2005), genetic screening should be individualised and is generally warranted in:

- Patients aged < 50 years, presenting with catecholamine secreting
- Multiple tumours
- Malignant tumours
- Bilateral tumours

Question 22

A 40 year old woman with a diagnosis of Addison's disease presents with persistent fatigue despite seemingly adequate replacement with glucocorticoids and mineralocorticoids. The role of dehydroepiandrosterone sulphates (DHEAS) is discussed during the consultation as she has read about this treatment and wondered if it might help her. Which of the following would best describe the impact of DHEAS from studies?

- **A)** Decreased weight
- **B)** Improved sense of well being
- **C)** Increase in muscle mass
- **D)** Increase in fertility
- **E)** Maintenance of blood pressure

Answer

Correct answer : Improved sense of well being

Dehydroepiandrosterone sulphates (DHEAS) are the androgens secreted by the adrenal glands, which decline with age. These were commonly termed as the elixir of youth with an alleged role in general well being, cognitive and sexual function and as a weight loss therapy. Randomised controlled trials have failed to demonstrate any apparent benefit with DHEAS in patients with normal adrenal function. These may play a role in female patients with adrenal insufficiency by increasing a sense of well being by bringing about a modest improvement in sexual function.

Question 23

A 65 year old woman is investigated for an assumed secondary hypertension. She has been found to have a blood pressure of 165/95 mmHg. There is little to find on examination and her BMI is 26.4 kg/m^2. Currently she takes amlodipine 10 mg daily. Results of her investigations are shown below.

		Normal Ranges
Sodium	143 mmol/L	(135-145)
Potassium	3.8 mmol/L	(3.5-5.5)
Urea	8 mmol/l	(3-8)
Creatinine	72 µmol/L	(60-115)
Plasma Renin Activity	0.5 nmol/L	(0.5-2.2)
Aldosterone	782 pmol/L	(100-500)

Which of the following is the most appropriate investigation for this patient?

- **A)** Adrenal CT
- **B)** Adrenal venous sampling
- **C)** Arrange MIBG scan
- **D)** Stop amlodipine and repeat the renin aldosterone ratio
- **E)** Postural stimulation test

Answer

Correct answer : Adrenal CT

This patient is likely to have Conn's syndrome. She has an elevated PRA:aldosterone ratio ~1500 but has a normal potassium that may confound some people. About 20% of patients with Conn's syndrome may have a normal potassium. Primary hyperaldosteronism accounts for as many as 10% of patients diagnosed to have essential hypertension in one secondary care hypertension clinic. Screening for excess aldosterone production is warranted in the following group of patients:

1. Young hypertensives (age <40
2. Resistant hypertension (unresponsive to 3 or more antihypertensive agents)
3. Associated hypokalaemia
4. Incidental adrenal tumour

Measurement of aldosterone: renin ratio is the best initial diagnostic test. Increased aldosterone and suppressed renin levels are highly indicative of underlying primary aldosteronism. A number of medications interfere with test results and should ideally be stopped. The following interfere with PRA: aldosterone interpretations and need to be stopped prior to assessing the ratio:

Aldosterone antagonists - spironolactone

Beta- blockers - lower PRA increase false positive results

A CT of the abdomen is usually the radiological modality employed to localise the adrenal adenoma. But as the incidence of adrenal incidentalomas rises with age, adrenal venous sampling is the technique most often used to confirm and lateralise the site of lesion. Considering this lady is 65 years old and her biochemistry reveals normal potassium and high sodium along with non usage of any of the interfering antihypertensive medications, the next investigation used should be a CT of the abdomen and adrenal venous sampling should be used only if there is a suspected adrenal adenoma. In view of her age group, she is more likely to have adrenal hyperplasia.

Question 24

A 70 year old male has a history of hypertension which is adequately controlled with doxazosin yet has persistent hypokalaemia. The patient is referred to clinic as the potassium is persistently between 2.6-3.1 mmol/l. Investigations show a plasma renin activity:aldosterone ratio of 780. Which of the following is the most appropriate management option for him?

- **A)** Switch Doxazosin to an ACE inhibitor
- **B)** Start a Potassium supplement
- **C)** Switch Doxazosin to spironlactone
- **D)** Switch Doxazosin to a Thiazide diuretic
- **E)** Stop Doxazosin

Answer

Correct answer : Start a Potassium supplement

The initial screening test for the diagnosis of primary aldosteronism is measurement of a plasma renin activity to aldosterone ratio. A ratio above 1000 is highly suggestive of primary hyperaldosteronism. (In the UK this is used and in the US they often quote the other way around i.e. aldo:renin ratio (ARR) where a ratio of >20 is suggestive of a diagnosis of primary aldosteronism). However false positives and negatives can occur. Some medications can interfere with aldosterone/ renin levels. Doxazosin has no effect. Also if the patient is hypokalaemic, aldosterone concentrations can fall and marginal increases in renin can make for a false negative result. Oral potassium supplements are given to avoid any false negative test results. A false negative result can also be obtained in patients with chronic renal failure due to persistently elevated renin levels.

Question 25

A 38 year old man is admitted after an RTA leading to head trauma. He is being managed in the intensive care unit. On day 2 of admission his 24 hour urinary free cortisol values are noticed to be high. You are asked to give an opinion regarding further assessment for his possible cortisol excess secretion.

What is the most appropriate next step in his management?

- **A)** Check mid night cortisol values
- **B)** Low dose DST
- **C)** Organise ODST
- **D)** No need to evaluate cortisol secretion at this stage
- **E)** Repeat 24 hour UFC

Answer

Correct answer : No need to evaluate cortisol secretion at this stage

In a critically ill patient CRH, ACTH and cortisol levels increase rapidly as a haemostatic response to the illness. Low cortisol binding globulin and albumin levels during the acute illness can cause an elevation of free cortisol levels. As a result, cortisol levels during an acute illness are not truly reflective of adrenal hypersecretion and a suspected adrenal excess cortisol values should only be evaluated (if clinically warranted) once the patient shows clinical improvement.

Question 26

You review a 25 year old man in clinic who has a diagnosis of congenital adrenal hyperplasia which was diagnosed at the age of 9. He takes dexamethasone 0.25 mg daily. Which of the following is the best investigation to monitor a patient with classic salt wasting congenital adrenal hyperplasia (CAH)?

- **A)** 17 hydroxyprogesterone (17 OHP) levels
- **B)** 21 alpha hydroxylase
- **C)** DHEA levels
- **D)** Measure plasma renin activity
- **E)** Plasma deoxycortisol

Answer

Correct answer : 17 hydroxyprogesterone (17 OHP) levels

Classic salt wasting congenital adrenal hyperplasia (CAH) is an autosomal recessive genetic disorder with a prevalence of 1: 10,000 - 1: 15,000. It is due to a deficiency of 21 alpha hydroxylase enzyme and usually presents with acute life threatening illness in a neonate with vomiting, dehydration, circulatory collapse and features of adrenal insufficiency on biochemistry but can also present later in life.

Management includes steroid replacement and about 3/4th of patients may require mineralocorticoid replacement in addition. Monitoring of treatment is based on clinical examination (signs of hyperandrogenism and glucocorticoid excess) and biochemical measurement of 17 OHP levels. Renin activity may also be used to monitor adequacy of replacement with associated mineralocorticoid deficiency - patient would be on fludrocortisone. The aim of steroid therapy is usually to keep 17 OHP levels mildly elevated (to prevent side effects related to excess steroid replacement) and fludrocortisone dose is titrated with the aim to keep plasma renin levels in mid normal range.

Question 27

A 24 year old man who presents with hypertension, hypokalaemia, suppressed renin and aldosterone values is suspected to have apparent mineralocorticoid excess. Which of the following tests can be used to establish the diagnosis?

- **A)** Check 3 β hydroxy steroid dehydrogenase (3 β HSD) enzyme levels
- **B)** CT abdomen
- **C)** Deoxycortisol levels
- **D)** Measure urinary cortisol to cortisone ratio
- **E)** Serum cortisol

Answer

Correct answer : Measure urinary cortisol to cortisone ratio

Presence of hypertension, hypokalaemia and suppressed renin and aldosterone values are suggestive of apparent mineralocorticoid excess seen due to deficiency of 11β hydroxy steroid dehydrogenase (11β HSD) enzyme in this patient. This enzyme mediates the conversion of cortisol to cortisone locally to protect mineralocorticoid receptor.

Deficiency of 11β HSD leads to hampered conversion of cortisol (which is a more potent mineralocorticoid as compared to cortisone) to cortisone locally, resulting in a state of apparent mineralocorticoid excess. The patients usually present with hypertension, hypokalaemia and metabolic alkalosis in presence of suppressed levels of aldosterone and renin. The diagnosis can be confirmed by measurement of urinary tetrahydrocortisol to cortisone ratio (increased levels of tetrahydrocortisol as compared to cortisone).

Question 28

You are called via the arrest bleep to a 43-year-old woman who is on the surgical ward. She had a laparoscopic cholecystectomy performed two days ago and has since had nausea and vomiting and has been receiving IV dextrose. It transpires that she had a fit for which the nursing staff requested the arrest team. She is now drowsy. Her past medical history is unremarkable.

On examination, she is drowsy with a GCS of 13. Her pulse is 88 bpm and blood pressure 132/88 mmHg with oxygen sats of 100% on air. There is no focal neurology and her plantar responses are equivocal.

Of note, her blood results reveal:

		Normal Ranges
Sodium	118 mmol/l	(135-144)
Potassium	3.5 mmol/l	(3.5-5)
Urea	3.8 mmol/l	(3-8)
Creatinine	70 micromol/l	(50-100)
Glucose	4.1 mmol/l	(3.5-6)

Which of the following is the most appropriate initial treatment for this patient?

- **A)** 15 mg oral Tolvaptan
- **B)** 100 mg IV hydrocortisone stat
- **C)** 150mls of 3% hypertonic saline over 20 mins
- **D)** 1 litre normal saline infused over 4 hrs
- **E)** Fluid restriction to 500mls per day

Answer

Correct answer : 150mls of 3% hypertonic saline over 20 mins

This patient is likely to have hyponatraemic encephalopathy which is life threatening and has presented with a fit. Post-operative hyponatraemia is not uncommon and is likely to be due to a combination of SIADH which develops in the post-op period and the infusion of inappropriate IVIs. The European Endocrine Society Guidelines on severe hyponatremic encephalopathy recommend a rapid correction of sodium by approximately 5 mmol/l. This can ameliorate the cerebral oedema that underlies this disorder.

For more information on how to correct and what would be the target see the following guidelines:

European Journal of Endocrinology (2014) Clinical Practice Guideline on the diagnosis and management of hyponatraemia,

Question 29

A 45-year-old man is investigated for difficult to treat hypertension. He has a aldosterone:renin ratio of 1560. A CT scan of the adrenals reveals a 0.5 mm left adrenal limb lesion. He undergoes adrenal venous sampling, the results of which are shown below:

	Right adrenal vein	Left adrenal vein	Peripheral
Aldosterone	12,000 pmol/l	2000 pmol/l	850 nmol/l
Cortisol	1200 nmol/l	1500 nmol/l	420 nmol/l

Which of the following is the correct interpretation of these results?

- **A)** Bilateral aldosterone secretion
- **B)** Left unilateral aldosterone secretion
- **C)** Normal results
- **D)** Right unilateral aldosterone secretion
- **E)** Uninterpretable as one of the adrenal veins has not been catheterised

Answer

Correct answer : Right unilateral aldosterone secretion

This patient has primary hyperaldosteronism and, although the CT suggests that there is a nodule on the left adrenal, the AVS suggests that there is hypersecretion of aldosterone from the right adrenal. Catheterisation of both adrenal veins seems to have been achieved as reflected by the cortisol concentrations being similar and high in both adrenal vein samples. The ratio of aldosterone: cortisol in the dominant side (A:C 10:1 on right and 1.3 on left) should be >4:1 and in this case it is roughly 8:1 confirming unilaterality. Thus, the recommendation here would be that the surgical target should be the right rather than the left. Discrepant results between CT and AVS is noted in 20%, hence the rationale for applying AVS in the direction of surgery.

Adrenal vein sampling in the diagnosis of aldosteronism; Authors: Deipolyi AR, Oklu R

Question 30

A GP refers a 23-year-old woman on the electronic portal whom he says has presented to him with fatigue. Blood pressure is 116/70 mmHg with no postural drop. There is no medical history of note but he is concerned about excluding a diagnosis of ‘Addison’s disease’ as there has been a case in the press recently where the GP practice was heavily criticised for its management of a case of Addison’s. He states in the letter that he does not necessarily need for the patient to be seen in clinic if he can be reassured that she doesn’t have Addison’s disease, and requests advice.

The GP has checked a random cortisol and found this to be 402 nmol/l (NR 9am cortisol 140 – 640). Which of the following would be the most appropriate approach to managing this query?

- **A)** Arrange an outpatient appointment
- **B)** Arrange for the patient to have a routine short synacthen test with the endocrine nurse
- **C)** Ask the GP to request a 9am cortisol and ACTH concentration
- **D)** Ask the GP to request adrenal autoantibodies
- **E)** Reassure the GP that the results indicate that the patient does not have Addison’s disease

Answer

Correct answer : Reassure the GP that the results indicate that the patient does not have Addison's disease

We are not told the exact timing of the cortisol sample and usually cortisol would be highest at 9am. However, the random cortisol result above 400 nmol/l argues against Addison's disease and the GP can be reassured that the patient does not have Addison's in the absence of convincing symptoms such as postural hypotension or pigmentation. A normal cortisol response to the short synacthen test would be above 450 nmol/l.

Cortisol - Specimen requirements

Some studies argue that a 9am cortisol above 300 nmol/l excludes adrenal insufficiency

Lee, M.T., Won, J.G.S., Lee, T.I., Yang, H.J., Da Lin, H. and Tang, K.T., 2003. The relationship between morning serum cortisol and the short ACTH test in the evaluation of adrenal insufficiency. Chinese Medical Journal (Taipei), 65(12), pp.580-587.

Question 31

A 40-year-old woman presents with hypertension and anxiety. Investigations confirm a diagnosis of phaeochromocytoma. She informs you that her maternal grandmother was diagnosed with an adrenal tumour and high blood pressure in her 50s but she knows little more about this as she died of the problem at age 60 ish. Her mother died of lung cancer at age 56. She was a smoker.

Her biochemistry reveals elevated urine catecholamines. Her U+Es, calcium and LFTs are all normal. Her MRI reveals a left sided 2.6 cm adrenal adenoma.

Which of the following, if any, genetic tests should be requested?

- **A)** MEN type 2
- **B)** None required. This is a sporadic phaeochromocytoma
- **C)** Succinate dehydrogenase type B and D mutational analysis
- **D)** TMEM127 mutational analysis
- **E)** vHL mutational analysis

Answer

Correct answer : TMEM127 mutational analysis

Genetic testing for pheochromocytoma should be undertaken in individuals with phaeo presenting:

- Before 45 years of age
- Multiple tumours
- Extra adrenal phaeos/paragangliomas
- Family history
- Malignancy

Up to 10% of phaeos may be due to genetic causes. Clues to the genetic cause may be in the history. SDH B and D mutations are found in younger age groups usually with paragangliomas/ extra-adrenal phaeos. MEN type 2 is expected at a younger age and with hyperparathyroidism and medullary thyroid Ca. NF-1 would be expected to display neurofibromas/café au lait patches and vHL associated with haemangiomas, often cerebellar/ophthalmic and renal Ca, again at a younger age group. Therefore in this middle aged woman with a rather tenuous, but still relevant family history of phaeo, TMEM127 mutation is the most probable cause. It is associated with unilateral disease often little family history and the disease occurring in middle age 40-45.

Lefebvre, M. and Foulkes, W.D., 2014. Pheochromocytoma and paraganglioma syndromes: genetics and management update. Current Oncology, 21(1), p.e8.

Question 32

A 52-year-old man is referred by his GP with difficult to control hypertension. He has an associated potassium concentration of 3.0-3.3 mmol/l (3.5-5). He is taking ramipril, bendrofluazide and amlodipine and his blood pressure is 156/92 mmHg.
A plasma renin activity to aldosterone ratio on this treatment is 1200 (aldosterone 800 pmol/l and PRA 0.7). A CT scan of his adrenals is reported as ‘a possible 6 mm adenoma is noted in the distal limb of the right adrenal gland’. Which of the following is the most appropriate approach to the management of this patient?

- **A)** Arrange adrenal vein sampling
- **B)** Characterise the lesion further with MRI
- **C)** Commence spironolactone
- **D)** Recommend adrenalectomy
- **E)** Repeat PRA/aldosterone ratio off ramipril

Answer

Correct answer : Arrange adrenal vein sampling

This patient has features and biochemistry suggesting primary hyperaldosteronism, with the PRA Aldo ration greater than 1000. The CT scan suggests a lesion in the right limb of the adrenal which does suggest Conn's syndrome but one cannot be absolutely certain of this, particularly as co-incidental lesions are detected in up to 5% of abdominal CT scans. Prior to consideration of surgery, the diagnosis of unilateral or bilateral secretion should be confirmed with adrenal vein sampling.

Deipolyi, A.R., Bailin, A., Wicky, S., Alansari, S. and Oklu, R., 2015. Adrenal Vein Sampling for Conn's Syndrome: Diagnosis and Clinical Outcomes. Diagnostics, 5(2), pp.254-271.

Question 33

A 64-year-old man attended clinic with a history of pallor, vomiting, palpitations and headaches. His past medical history included paroxysmal atrial fibrillation (AF), type 2 diabetes and concentric left ventricular hypertrophy (LVH). He takes losartan, amlodipine, atorvastatin, omeprazole, amiodarone, warfarin, furosemide, betahistine and thyroxine. His sister had a pheochromocytoma and underwent adrenalectomy when she was 40. His blood pressure was 150/99 mmHg with the rest of the observations being normal. His systemic examination was entirely normal. Further testing revealed the following:

		Normal Ranges
Noradrenaline output [24hr urine]	2000 nmol/24h	(100-660)
Adrenaline output [24hr urine]	400 nmol/24h	(15-160)
Normetadrenaline output [24hr urine]	7.60 umol/24h	<4.00
Metadrenaline output [24hr urine]	3.43 umol/24h	<2.00

His CT scan showed a 6.5 x 4.8cm benign looking right sided adenoma and no metastasis elsewhere. He underwent laparoscopic right adrenalectomy for phaeochromocytoma. Subsequently, genetic testing demonstrated a heterozygous frameshift mutation in exon 4 of the TMEM127 gene and his sister was positive for the same gene. What investigations would you perform in follow up screening visits?

- **A)** Urinary catecholamines and CT adrenals
- **B)** Urinary catecholamines and CT thoracic, pelvis and abdomen
- **C)** Urinary catecholamines and MRI adrenals
- **D)** Urinary catecholamines and MRI skull base to pelvis
- **E)** Urinary catecholamines only

Answer

Correct answer : Urinary catecholamines and MRI adrenals

Explanation:

This is hereditary phaeochromocytoma/paraganglioma syndrome secondary to a germline mutation in the TMEM127 gene. It is a very rare condition. Phaeochromocytomas and paragangliomas are genetically heterogeneous neural crest-derived neoplasms. Germline mutations of FP/TMEM127 are associated with phaeochromocytomas but not paragangliomas. Therefore, a full body MRI is not needed for follow-ups.

Question 34

A 40-year-old woman presents to clinic with a six month history of palpitations, sweats, headaches and anxiety. There was nothing else of note in her clinical history and she took no medication. In her family history, her father died of kidney cancer when he was 48-years-old but he was a smoker.

On examination, she looked well and had a blood pressure of 156/98 mmHg. There was nil of note on abdominal examination.

Investigations revealed:

- **Urine Metadrenaline:** 4.2 µmol/24 h (<1.3)
- **MRI abdomen:** 3 cm right adrenal mass. 4 cm cyst in head of pancreas and smaller cysts of 6-8 mm in tail of pancreas. 4 mm right upper pole cortical cyst on right kidney without any other abnormality of kidneys.

Which of the following is the most likely diagnosis?

- **A)** multiple endocrine neoplasia type 2
- **B)** SDH type B-associated phaeochromocytoma–paraganglioma syndrome
- **C)** sporadic phaeochromocytoma
- **D)** TMEM phaeochromocytoma syndrome
- **E)** von Hippel–Lindau syndrome

Answer

Correct answer : von Hippel–Lindau syndrome

Explanation:

vHL is an autosomal dominant condition associated with the development of multiple haemangiomas in CNS/retina together with renal carcinoma and phaeochromocytoma. The diagnosis of phaeochromocytoma with elevated metadrenaline and symptoms in a person less than 50 should make one suspect a potential genetic contribution. In this case the fact that her father died of renal cell carcinoma should make one suspect vHL.

Reference:

- Gulani, A.C. et al. (2019) von Hippel-Lindau Disease.
- Dias Pereira, B., Nunes da Silva, T., Bernardo, A.T., César, R., Vara Luiz, H., Pacak, K. and Mota-Vieira, L., 2018. A Clinical Roadmap to Investigate the Genetic Basis of Pediatric Pheochromocytoma: Which Genes Should Physicians Think About?. International journal of endocrinology, 2018.

Question 35

A 40-year-old woman was referred with a lump on the left side of her neck. She also explains that she encounters diarrhoea and flushing. In her past history she was diagnosed with a right sided phaeochromocytoma 10-years-ago and had been under review by the surgical team up until 5-years-ago when she was discharged. She takes no medication and there is no family history of note.

On examination, there is a 3 cm lump on the left side of the thyroid. Blood pressure is 120/80 mmHg.

Calcitonin: 42 ng/l (<6)

Which of the following would you request in this patient?

- **A)** 1 mg overnight dexamethasone test
- **B)** DHEA
- **C)** Fasting gut peptides
- **D)** Parathyroid hormone
- **E)** Thyroid function tests

Answer

Correct answer : Parathyroid hormone

Explanation:

This patient has a previous phaeochromocytoma and thyroid mass with elevated calcitonin suggesting a medullary thyroid carcinoma. The suggested diagnosis therefore is MEN type 2 and the most relevant investigation would be to assess for hyperparathyroidism which is associated with MEN type 2a. The gene responsible has been identified as the RET proto-oncogene.

Reference:

- Daly, P.A. (2019) Multiple Endocrine Neoplasia, Type 2A (MEN 2A).

Question 36

A 22-year-old female attends clinic. She has a 6 year history of addison's disease and has had 3 hospital admissions due to adrenal crisis over the last 6 months. She is an avid runner and has more recently taken to training for a marathon. Prior to that she had been doing very well. She takes hydrocortisone 10 mg bd together with fludrocortisone 100 µg od. She denies any non-compliance with treatment. She describes her periods as generally normal.
On examination, she was slim, her pulse was 76 bpm regular and blood pressure was 104/60 mmHg. Investigations reveal:
Urea

Sodium	133 mmol/l	(134-144)
Potassium	5.0 mmol/l	(3.5-5)
5 mmol/l	(3-8)	
Creatinine	98 µmol/l	(50-100)
Free T4	13.1 pmol/l	(9-20)
TSH	1.8 mu/l	(0.5-4.5)

Which of the following is the most appropriate approach to the management of this patient?

- **A)** Advise the use of saline tablets during longer runs
- **B)** Check estradiol/LH/FSH and advise the combined oral contraceptive
- **C)** Increase dose of fludrocortisone to 150 µg daily
- **D)** Increase dose of hydrocortisone to 10 mg tds
- **E)** Switch hydrocortisone to prednisolone 5 mg daily

Answer

Correct answer : Increase dose of fludrocortisone to 150 µg daily

Explanation

A good point of note here is the fact that the patient has a pulse of 80 yet is a marathon runner – one would expect a pulse of maybe 50 – not 80. Thus, this patient appears to require a higher dose of fludrocortisone as suggested by the lower sodium concentration and admissions with ‘addison’s crisis’. This may be because of the increased salt losses associated with longer duration running and relative hypovolaemia. During a race, one can also consider increasing the dose of hydrocortisone by around 5 mg. There is no requirement here to increase the dose to 30mg daily as a continuous dose.

Reference

- Husebye, E.S., et al., (2014). Consensus statement on the diagnosis, treatment and follow-up of patients with primary adrenal insufficiency. Journal of Internal Medicine, 275(2), pp.104-115.

Question 37

A 78-year-old male was admitted with a 2 day history of deteriorating abdominal pain, and diarrhoea. He had a past medical history of polymyalgia rheumatica for which he took prednisolone 3 mg daily reduced gradually over the last year from 20 mg daily. On examination, he had a temperature of 39oC, a pulse of 110 bpm reg and a blood pressure of 120/74 mmHg. He had marked tenderness in the left iliac fossa with scant bowel sounds. CT abdomen revealed an acute diverticular abscess. He was treated with IV antibiotics.
How should his steroid dose be managed?

- **A)** Check urgent cortisol and, if above 200 nmol/l, can then stop steroids as they are a risk for bowel perforation
- **B)** Continue on current oral dose of prednisolone
- **C)** Increase the dose of prednisolone to 10 mg daily
- **D)** Switch prednisolone to IV hydrocortisone 50 mg qds
- **E)** Switch prednisolone to oral dexamethasone

Answer

Correct answer : Switch prednisolone to IV hydrocortisone 50 mg qds

Explanation

This patient may well have adrenal suppression based on the cumulative dose of steroids. Therefore he should receive IV hydrocortisone as above until the patient has made a recovery from the acute illness. Going forward the patient can be investigated at a later stage to assess for adrenal recovery with a short synacthen test.

Reference

- Society of Endocrinology (2019) Adrenal Crisis Information

Question 38

A 50-year-old female is admitted with a 1 week history of deteriorating lethargy, vomiting and fatigue. A short synacthen test reveals a peak cortisol response of 230 nmol/l (>450) 30 mins after synacthen. She is treated with hydrocortisone 10 mg twice daily and has a good response. Before discharge, which of the following should she also receive?

- **A)** An emergency supply of fludrocortisone
- **B)** An emergency supply of oral prednisolone
- **C)** An emergency hydrocortisone injection pack
- **D)** An oral emergency hydrocortisone pack
- **E)** Saline tablets

Answer

Correct answer : An emergency hydrocortisone injection pack

Explanation

All patients with a diagnosis of hypoadrenalism should be counselled on the recognition and management of acute hypoadrenalism and receive a parenteral IM/IV emergency hydrocortisone supply.

Reference

- Pituitary Foundation (2018) Treating a pituitary condition - hydrocortisone

Question 39

A 28-year-old woman is a known-case of primary adrenal insufficiency (autoimmune aetiology). She has no history of any other autoimmune disorders. The patient is currently on hydrocortisone dose of a total of 25 mg in a day (15 mg in the morning, 5 mg in the afternoon, 5 mg in the evening) along with 100 mcg of fludrocortisone. The patient is comfortable with the current doses of the medications. She is otherwise asymptomatic at present. She has come to you because she is pregnant with the current estimated gestational age of 8 weeks based on her last menstrual period.

What advice should be given to her regarding the management of her adrenal insufficiency?

- **A)** Both the doses of hydrocortisone and fludrocortisone should be preemptively increased
- **B)** The decision to increase the dose of hydrocortisone or fludrocortisone must be based on Cortisol levels and plasma renin activity, respectively
- **C)** The dose of fludrocortisone should be increased preemptively while keeping the dose of hydrocortisone intact
- **D)** The dose of hydrocortisone should be increased preemptively keeping the dose of fludrocortisone intact
- **E)** The doses of neither of the medications should be preemptively increased in the first trimester. The patient should be kept on a regular follow-up and symptoms and signs suggestive of under-replacement of glucocorticoids and/or mineralocorticoids must be monitored

Answer

Correct answer : The doses of neither of the medications should be preemptively increased in the first trimester. The patient should be kept on a regular follow-up and symptoms and signs suggestive of under-replacement of glucocorticoids and/or mineralocorticoids must be monitored

Explanation:

In a normal pregnancy, the free cortisol levels typically increase after 22-24 weeks of pregnancy. Hence, the dose of hydrocortisone is increased by 20-40% in the patients after 22-24 weeks of pregnancy. Whether this increased after 22-24 weeks must be done pre-emptively or selectively is debated. (Bornstein et al., 2016)

Progesterone has an anti-mineralocorticoid effect. Despite this, the dose of fludrocortisone is not typically increased. Hydrocortisone has a good mineralocorticoid effect, and hence the increase of the dose of hydrocortisone may cover the increased mineralocorticoid requirement.(Bornstein et al., 2016) Besides this, fludrocortisone falls in Pregnancy category C and therefore increase of the dose of the medication is not without risk. (Oliveira et al., 2018)

Our patient is currently in the first trimester, and she is asymptomatic. There is no evidence to suggest under-replacement of either glucocorticoids or mineralocorticoids at present. Hence it is advisable to keep a close watch on the patient clinically and to consider dose escalation if the patient has clinical features suggestive of under-replacement like failure to gain weight, hypotension, excessive nausea or vomiting.

The total cortisol values increase physiologically in the pregnancy because of the increase of cortisol binding globulin. In the absence of free cortisol measurement, the interpretation of the total cortisol values in pregnancy may be difficult. The plasma renin activity also increases physiologically in pregnancy.(Bornstein et al., 2016)

Reference:

- Bornstein, S. R. et al. (2016) ‘Diagnosis and treatment of primary adrenal insufficiency: an endocrine society clinical practice guideline’, The Journal of Clinical Endocrinology & Metabolism. Oxford University Press, 101(2), pp. 364–389
- Oliveira, D. et al. (2018) ‘Treatment of Addison’s disease during pregnancy’, Endocrinology, diabetes & metabolism case reports. Bioscientifica Ltd, 2018(1)

Question 40

A 60-year-old female is seen in the adrenal adenoma clinic. She has a CT colonoscopy for abdominal pain, which was reported as normal from the GI perspective, but a co-incidental note was made of a left 2.4 cm adrenal adenoma. She has a background of hypertension and takes atorvastatin and amlodipine together with topiramate prescribed by neurology for migraine. She also takes thyroxine 50 micrograms daily for a 20-year history of primary hypothyroidism. Otherwise, she is well.

There is little of note on examination, other than she is obese with a body mass index (BMI) of 33 kg/m^2, her blood pressure is 136/80 mmHg but she has no overt endocrinopathy.

Investigations reveal normal Panel Reactive Antibodies (PRA): Aldosterone ratios, repeat CT scan of the adrenals performed 3 months later is unchanged, and her urine catecholamine concentrations are normal. Her 1mg overnight dexamethasone suppression test reveals a 9 am Cortisol of 140 nmol/l (<50).

Further investigation shows:

Urine free cortisol is 138 nmol/d (<150) and her ACTH concentration is 20.3 ng/l (10-50).

She undergoes a low-dose dexamethasone test and the 48hr 9 am cortisol is 130 nmol/l.

Which of the following is the most appropriate test for this patient?

- **A)** Arrange adrenal vein sampling with ACTH stimulation
- **B)** Arrange inferior petrosal sinus sampling
- **C)** Arrange MRI of pituitary
- **D)** Measure dexamethasone levels with cortisol on further 1mg overnight dexamethasone test
- **E)** Refer to endocrine/surgical MDT for consideration of adrenalectomy

Answer

Correct answer : Measure dexamethasone levels with cortisol on further 1mg overnight dexamethasone test

Explanation:

This patient presents with what appears to be co-incidental adrenal adenoma and an endocrine investigation reveals non-suppressible cortisol, yet the urine free cortisol is normal and the ACTH is also normal. The normal ACTH would make one suspicious of this being pituitary-driven Cushing's disease rather than this being due to an adrenal adenoma as the ACTH would be expected to be low in the latter. However, the patient does not appear to be cushingoid from the examination report and is taking topiramate for migraine. This is an inducer of liver enzymes speeding up the metabolism of dexamethasone. Therefore, the most appropriate next step would be to repeat the dexamethasone suppression test with measurement of dexamethasone concentrations and a level less than 5 mmol/l is associated with rapid metabolism of the dexamethasone probably due to topiramate and hence an inability to rely on this result.

Reference:

- Åsvold, B.O., Grill, V., Thorstensen, K. and Bjørgaas, M.R., 2012. Association between post-test dexamethasone and cortisol concentrations in the 1 mg overnight dexamethasone suppression test. Endocrine connections, 1(2), pp.62-67

Question 41

A 38-year-old female was referred by her GP to an endocrine clinic for evaluation of palpitations, sweating, shortness of breath and headaches that occurred every few days. Her blood pressure was 180/110 mmHg and she had visible thyroid swelling. Her past medical history was significant for renal cell carcinoma.
Lab evaluation revealed:

Test	Result	Normal range
Urinary normetadrenaline	7.2umol/ 24 hours	(<4.00)
Urinary metadrenaline	18umol/ 24 hours	(<2.00)
Serum TSH	0.35mU/L	(0.35-5.5)
PTH	4.5pmol/L	(1.6-7.2)
Corrected calcium	2.31mmol/L	(2.2-2.6)

Which of the following genetic mutations is associated with her clinical profile?

- **A)** NF1
- **B)** RET proto-oncogene
- **C)** SDHB
- **D)** SDHD
- **E)** TMEM127

Answer

Correct answer : SDHB

Explanation:

The presence of palpitations, headache and sweating in a patient with hypertension should raise the diagnostic query of pheochromocytoma. Moreover, patients may present with pallor or flushing, apprehension, chest pain, dyspnea, constipation and paroxysmal thyroid swelling. Pheochromocytomas (aPCA) are chromaffin tumours arising from the adrenal medulla and secrete catecholamines, while paragangliomas are tumours arising from extra-adrenal sympathetic or parasympathetic nervous tissue. Sympathetic paraganglia tumours are termed as extra-adrenal functional paraganglioma (eFPGL) whereas parasympathetic paraganglia tumours are referred to as head and neck paraganglioma (HNPGL). Currently, 25% of patients with apparently sporadic pheochromocytoma are found to have an underlying genetic mutation with the presence of associated conditions e. g. RET mutations (20%) and co-incident medullary thyroid cancer, VHL mutation (45%) and co-incident angiomas, NF1 mutation with café-au-lait spots and cutaneous neuromas. Succinate dehydrogenase (SDH) enzyme consists of four subunits (A, B, C and D). Mutations in SDHB (17%), SDHD (18%) and SDHC may cause aPCA, eFPGL and HNPGL, while SDHA mutation rarely causes, but is associated with juvenile encephalopathy. SDHB mutation is associated with a more malignant phenotype and has the potential for recurrent malignant and extra-adrenal tumours such as renal cell carcinoma. TMEM127 mutation should be considered in patients with pheochromocytoma after a negative screening of VHL, RET, SDHB and SDHD genes.

Although urinary metanephrines are specific for the diagnosis of pheochromocytoma, screening for associated conditions should be performed either by looking for associated clinical manifestations or by genetic testing.

Reference:

- Wass, J. and Owen, K. (2014) Oxford handbook of Endocrinology and Diabetes. 3rd edn. Pakistan: Oxford University Press. (Book)
- Karasek, D., Frysak, Z. and Pacak, K., 2010. Genetic testing for pheochromocytoma. Current hypertension reports, 12(6), pp.456-464.

Question 42

A 52-year-old female with diet-controlled type 2 diabetes mellitus was seen in the emergency department with diffuse abdominal pain and vomiting. On examination, her blood pressure was 120/80 mmHg and her pulse rate was 70/min. The rest of her examination was unremarkable. A CT scan was obtained. However, the pain resolved two hours after the presentation.
Blood studies revealed:

Test	Result	Normal Range
Sodium	139mEq/L	(135-145)
Potassium	4.1mEq/L	(3.5-4.5)
Urea	5mg/dL	(7-20)
Creatinine	90umol/L	(60-115)
Calcium (corrected)	2.25mmol/L	(2.2-2.6)

CT scan: 2 cm well-circumscribed right adrenal mass with a density of 5 Hounsfield units.
In addition to plasma free metanephrine levels, what is the most appropriate diagnostic test to perform?

- **A)** 17a oestradiol
- **B)** Adrenal vein sampling
- **C)** Aldosterone/renin ratio
- **D)** Low dose dexamethasone suppression test
- **E)** Urinary metanephrines

Answer

Correct answer : Low dose dexamethasone suppression test

Explanation:

Adrenal incidentaloma is an adrenal mass that is discovered incidentally upon imaging carried out for reasons other than a suspected adrenal pathology. Imaging studies suggest that adrenal masses are present in 2-3% of the general population. Incidence increases with age as 8-10% of 70-year olds harbour an adrenal mass. 85-90% of these adrenal masses are non-functional while 10-15% are functioning, of which, pheochromocytoma and cortisol secreting adrenal adenoma causing Cushing's syndrome or subclinical Cushing's syndrome have been reported as an underlying diagnosis.

Any patient with adrenal incidentaloma measuring <4cm with benign radiological features (homogeneous mass, well-defined borders and <10HU on a non-contrast CT) should undergo clinical and biochemical evaluation to assess the functional status of the lesion. All patients should have plasma free metanephrine levels to rule out pheochromocytoma. Plasma metanephrines are the most sensitive screening test for detection of catecholamines excess and have slightly lower specificity than urinary metanephrines which may be used for confirmation if plasma metanephrines are borderline. An overnight dexamethasone suppression test is the preferred screening test to rule out Cushing's syndrome. An aldosterone to renin ratio test to rule out Conn's syndrome is completed only if the patient is hypertensive. Adrenal vein sampling is indicated with bilateral adrenal changes. It is the gold standard for differentiation between uni and bilateral aldosterone production. 17 oestradiol levels are checked only in females if adrenal carcinoma is suspected.

Reference:

- Wass, J. and Owen, K. (2014) Oxford handbook of Endocrinology and Diabetes. 3rd edn. Pakistan: Oxford University Press. (Book)
- Gendy, R. and Rashid, P., 2017. Incidental adrenal masses-a primary care approach. Australian family physician, 46(6), pp.385-390.

Question 43

A 15-year-old female was referred to the endocrine clinic for evaluation of hypertension fluctuating from 150/90 to 170/100 mmHg and hypokalaemia fluctuating from 2.8 to 3.1mmol/L over the last year. Two months ago, she started experiencing headaches, dizziness and fatigue. Her blood pressure was 180/110mmHg. There was no abnormality in her secondary sexual characteristics development.
Further blood tests revealed:

Test	Result	Normal Range
Sodium	146mmol/L	(135-145)
Potassium	2.2mmol/L	(3.5-5.5)
Venous bicarbonate	32mEq/L	(18-25)
Random plasma aldosterone concentration (PAC)	68pmol/L	(100-850)
Random plasma renin activity (PRA)	0.2pmol/mL/hr	(0.5-3.1)
Cortisone level	low	

Based on her clinical features and biochemical profile, which enzyme is most likely deficient that is consistent with this underlying diagnosis?

- **A)** 11 ß-hydroxylase
- **B)** 11 ß-hydroxysteroid dehydrogenase (HSD) type 1
- **C)** 11 ß-hydroxysteroid dehydrogenase (HSD) type 2
- **D)** 17 a-hydroxylase
- **E)** 21 a-hydroxylase

Answer

Correct answer : 11 ß-hydroxysteroid dehydrogenase (HSD) type 2

Explanation:

Hypertension, in association with hypokalaemic alkalosis, are features of hyperaldosteronism. Occasionally, the clinical syndrome of hyperaldosteronism is not associated with excess aldosterone, as in this case. This can be either due to an increase in alternative mineralocorticoid or due to an increased mineralocorticoid effect of cortisol.

The mineralocorticoid receptor has an equal affinity for cortisol and aldosterone and is usually protected from the effects of stimulation by cortisol by 11ß-hydroxysteroid dehydrogenase (HSD) enzyme type 2, which converts cortisol to cortisone. In apparent mineralocorticoid excess (AME), there is a deficiency of 11ß-HSD type 2 enzyme. This can be due to congenital absence of enzyme or by inactivating mutations in the 11 ß-HSD2 gene or due to exogenous intake of substances that inhibit 11 ß-HSD2 such as liquorice or carbenoxolone. This results in increased cortisol stimulation of mineralocorticoid receptors and leads to severe hypertension along with hypokalemic alkalosis and suppression of renin and aldosterone. 11 ß-HSD1 converts cortisone to cortisol and its deficiency results in increased levels of cortisone. 17 a-hydroxylase and 11ß-hydroxylase deficiency leads to excess production of deoxycorticosterone (DOC) which acts as an agonist at the mineralocorticoid receptor resulting in congenital adrenal hyperplasia, hypertension and suppression of renin. 21a-hydroxylase deficiency results in aldosterone and cortisol deficiency with ACTH hypersecretion due to loss of -ve feedback from cortisol. This results in adrenocortical hyperplasia and increased androgen synthesis (testosterone and androstenedione) leading to sexual dysfunction and subfertility.

Reference:

- Wass, J. and Owen, K. (2014) Oxford handbook of Endocrinology and Diabetes. 3rd edn. Pakistan: Oxford University Press. (Book)
- Palermo, M., Quinkler, M. and Stewart, P.M., 2004. Apparent mineralocorticoid excess syndrome: an overview. Arquivos Brasileiros de Endocrinologia & Metabologia, 48(5), pp.687-696.

Question 1

A 16 year old boy has a 3 year history of type 1 diabetes and has a HbA1c of 66.1 mmol/mol (8.2%) (<42.1 mmol/mol (6)), requiring his mother to administer his insulin due to his poor eyesight, a consequence of optic atrophy. He also has sensorineural deafness and requires a hearing aid. His current medication includes basal bolus insulin regime consisting of insulin aspart tds and insulin glargine together with desmopressin bd. He has an average self monitored glucose profile of 7.6 mmol/l.

Which of the following is the likely diagnosis?

- **A)** Alport syndrome
- **B)** Alstrom syndrome
- **C)** Kearns-Sayre syndrome
- **D)** MELAS syndrome
- **E)** Wolfram Syndrome

Answer

Correct answer : Wolfram Syndrome

This patient expresses the clinical features of The DIDMOAD or Wolfram syndrome, characterised by, diabetes insipidus (the patient takes desmopressin), diabetes mellitus of juvenile onset, optic atrophy and deafness. Diabetes occurs in nearly all patients presenting with this syndrome. While little is known around the specific cellular mechanisms, pancreatic islets from such patients demonstrate a selective absence of beta cells suggesting an underlying mechanism involving programmed beta cell death/apoptosis as there are no immunological markers.

Question 2

A 41 year old man with a history of diabetes secondary to chronic alcohol related pancreatitis is reviewed in clinic. On examination his BMI is 22 kg / m^2 , his body weight is 69 kg and his blood pressure is 124 / 66 mmHg. He has no evidence of retinopathy on fundoscopy and examination of his feet reveals no evidence of neuropathy. His current medication includes humalog mix 25 twice daily at doses of 10 and 6 units respectively. His current Hba1c is 62.8 mmol/mol (7.9%) (<42.1 mmol/mol (6)) and his main complaints are persisting episodes of diarrhea, frequent hypoglycaemic episodes with great variability in his self monitored blood glucose levels.

Which of the following is the likely cause of these symptoms for this gentleman?

- **A)** Exocrine pancreatic insufficiency, reduced glucagon and insulin secretion with increased hepatic glucose production and increased insulin resistance
- **B)** Exocrine pancreatic insufficiency, reduced insulin secretion, increased glucagon secretion with increased insulin resistance
- **C)** Exocrine pancreatic insufficiency, reduced insulin and glucagon secretion with reduced hepatic glucose production and increased insulin sensitivity
- **D)** Normal pancreatic exocrine function, reduced insulin secretion, increased glucagon secretion with reduced insulin sensitivity
- **E)** Exocrine pancreatic insufficiency, reduced insulin secretion, normal glucagon secretion, increased hepatic glucose production with reduced insulin sensitivity.

Answer

Correct answer : Exocrine pancreatic insufficiency, reduced insulin and glucagon secretion with reduced hepatic glucose production and increased insulin sensitivity

This patient has minimal insulin requirements (0.2 u / kg) while complaining of recurrent diarrhea with evidence of glucose instability. The pathophysiology of diabetes secondary to pancreatic injury results in both exocrine and endocrine pancreatic insufficiency. The exocrine pancreatic insufficiency results in malabsorption, diarrhea and contributing to glucose instability. Endocrine pancreatic insufficiency in such patients results in reduced insulin and glucagon secretion with consequent reduction in hepatic glucose production resulting in an increase in insulin sensitivity. Furthermore the glucagon deficiency that occurs in such patients also results in elevations in urea cycle amino acids in particular alanine, asparagine, cysteine, glycine, proline and serine. These metabolic features contribute to the glucose fluctuations that occur in patients with diabetes secondary to pancreatic injury and provide considerable clinical challenges.

Question 3

A 32 year old man is referred by his GP. He was diagnosed with diabetes at the age of 14 and initially treated with metformin and was commenced on exogenous insulin at the age of 22. He has a long standing history of obesity and has difficulty in glucose monitoring due to very poor vision, having had deterioration in vision from the age of 8.

On examination his BMI is 44 kg / m^2 , his body weight is 132 kg, his blood pressure is 150/78 mmHg, he has acanthosis nigricans in axillae and nape of neck, reduced vibration sensation in both feet and also evidence of sensorineural deafness. His current medication includes Novomix 30 84 units twice daily, ramipril 5 mg daily and atorvastatin 40 mg once daily

Investigations reveal:

		Normal Ranges
Hba1c	70.5 mmol/mol	(8.6%)
Total Cholesterol	5.7 mmol/l	(<5)
Fasting plasma triglyceride	9.8 mmol/l	(0.9 - 2.2)
U + Es	Normal	
AST	78 iu/l	(5 - 45)
ALP	138 iu/l	(30 - 115)
eGFR	94 ml/min/1.73 m^2	(90 - 110)
TSH	1.2 mu/l	(0.32 - 5.5)

What is the correct diagnosis for this patient?

- **A)** Alström syndrome
- **B)** Bloom syndrome
- **C)** Edwards syndrome
- **D)** Glycogen storage disease
- **E)** MELAS syndrome

Answer

Correct answer : Alström syndrome

Alström syndrome (AS) is a rare autosomal recessive disease characterized by multiorgan dysfunction. The key features are childhood obesity, blindness due to congenital retinal dystrophy, and sensorineural hearing loss. Associated endocrinologic features include hyperinsulinemia, early-onset type 2 diabetes, and hypertriglyceridemia. Thus, AS shares several features with the common metabolic syndrome, namely obesity, hyperinsulinemia, and hypertriglyceridemia. Mutations in the ALMS1 gene have been found to be causative for AS with a total of 79 disease-causing mutations having been described. Further symptoms described in relation to AS include progressive sensori neural hearing loss, a dilated cardiomyopathy in over 60% of cases, developmental delays in 50 % of cases leading to learning difficulties in up to 30% of cases. MELAS syndrome describes a mitochondrial myopathy associated with type 2 diabetes, lactic acidosis, encephalopathy and stroke like episodes. Bloom syndrome is another insulin resistant syndrome being associated with an impaired glucose tolerance and IUGR. Glycogen storage disease is a condition associated with impaired glucose tolerance, hepatomegaly and may be a cause of early hypoglycemia.

Question 4

A 42 year old South Asian man is referred to the diabetic clinic by his GP. He has a 5 year history of type 2 diabetes. He complains of feeling tired and has a previous history of ischaemic heart disease. On examination his BMI is 34 kg/m^2, his pulse is 51 bpm and his blood pressure is 148 / 78 mmHg. His current medication includes 'Novomix 30' 42 units twice daily, metformin 500 mg twice daily, simvastatin 20 mg once daily, aspirin 75 mg once daily, enalapril 20 mg once daily and atenolol 50 mg once daily.
Investigations reveal:

		Normal Ranges
HbA1c	62.8 mmol/mol (7.9%)	(<42.1 mmol/mol (6))
Total Cholesterol	5.6 mmol/l	(<5)
LDL-Cholesterol	3.7 mol/l	(< 3)
Plasma Triglyceride	2.2 mmol/l	(0.9 - 2.2)
TSH	16.8 mu / l	(0.32 - 5.5)
Free T4	7.9 pmol/l	(9.4 - 23.4)

Which of the following is the most appropriate approach to optimise this patient's lipid profile?

- **A)** Commence fenofibrate
- **B)** Commence Omega-3 fish oil
- **C)** Commence thyroxine
- **D)** Improve glycaemic control
- **E)** Increase simvastatin dose

Answer

Correct answer : Commence thyroxine

This patient is hypothyroic as evidenced by the low T4 and elevated TSH. Correction of his thyroid status will contribute to an improvement in his lipid profile. Increasing the statin dose or commencing a fibrate is not appropriate as hypothyroidism is a risk factor for lipid lowering therapy-associated myotoxicity. Omega-3 fish oils are not routinely recommended for use in this setting.

Question 5

A 33 year old lady with a 10 year history of type 1 diabetes has been converted from twice daily Novomix to a basal bolus insulin regimen comprising of insulin glargine and novorapid three months previously at a total daily dose of 72 units. On review in the clinic her glycaemic control has improved since her insulin regimen change with her current Hba1c measuring 65 mmol/mol (8.1 %) (<42.1 mmol/mol (6)) compared with 73.8 mmol/mol (8.9%) (<42.1 mmol/mol (6)) prior to her regimen change. She is however unclear as to how to modify her prandial insulin doses according to her diet.

Which of the following is the most appropriate initial advice for this lady with respect to adjusting her prandial insulin dose?

- **A)** 0.5 units of insulin per 10 grams of dietary carbohydrate
- **B)** 1 unit of insulin per 10 grams of dietary carbohydrate
- **C)** 2 units of insulin per 10 grams of dietary carbohydrate
- **D)** 3 units of insulin per 10 grams of dietary carbohydrate
- **E)** 4 units of insulin per 10 grams of dietary carbohydrate

Answer

Correct answer : 1 unit of insulin per 10 grams of dietary carbohydrate

The DAFNE patient education program suggests that patients should initially adjust prandial insulin doses by 1 unit according to each 10 grams of dietary carbohydrate. This initial ratio may subsequently be modified according to response and the influence of other factors such as exercise.

Question 6

A 40 yr old woman presents to her GP with recurrent vaginal thrush. She has a previous history of hypothyroidism and is receiving long term thyroxine replacement. On examination, her BMI is 30 kg / m^2 and her blood pressure is 144/85mm Hg. Investigations reveal a fasting plasma glucose of 13 mmol/l (<5.6) and an HbA1c of 74.9 mmol/mol (9%) (<42.1 mmol/mol (6)).

Which of the following would favour a diagnosis of type 2 rather than type 1 diabetes for this lady?

- **A)** Autoimmune aetiology of hypothyroidism
- **B)** High LDL cholesterol level
- **C)** High HDL cholesterol level
- **D)** Normal albumin/creatinine ratio
- **E)** Presence of background retinopathy

Answer

Correct answer : Presence of background retinopathy

Type 1 diabetes is associated with the presence of islet cell antibodies along with other autoimmune conditions. HDL-C concentrations are higher in patients with type 1 diabetes, while up to 20% of patients with type 2 diabetes will demonstrate evidence of microvascular complications at diagnosis which will not be the case in patients with type 1 diabetes.

Question 7

A 69 year old man has a 7 year history of type 2 diabetes is reviewed in clinic. His current medication includes metformin 1 gram twice daily, gliclazide 160 mg twice daily, simvastatin 20 mg once daily, ramipril 5 mg once daily and aspirin 75 mg once daily. On examination his BMI is 31 kg / m^2 his blood pressure is 145 / 86 mmHg and he has no clinical evidence of microvascular complications. His most recent Hba1c is 44.3 mmol/mol (6.2%) (<42.1 mmol/mol (6)). His main complaint is that of feeling continually hungry and he has experienced pre-syncopal like symptoms associated with capillary blood glucose measurements of between 2.5 and 3.5mmol/l.

Which of the following is a feature of hypoglycaemia in patients with type 2 diabetes?

- **A)** 15% of patients with type 2 diabetes experience disabling hypoglycaemia within 2 years of initiation on a basal insulin
- **B)** 2% of patients receiving sulphonylurea therapy experience severe hypoglycaemia
- **C)** Approximately 10% of patients with type 2 diabetes experience symptomatic hypoglycaemia
- **D)** The prevalence of severe hypoglycaemia is higher in patients recently commenced on a basal insulin than in patients receiving sulphonylurea therapy.
- **E)** The prevalence of severe hypoglycaemia is similar in patients with type 2 diabetes receiving insulin for more than 5 years to that in patients with type 1 diabetes

Answer

Correct answer : The prevalence of severe hypoglycaemia is similar in patients with type 2 diabetes receiving insulin for more than 5 years to that in patients with type 1 diabetes

Data from UKPDS and the RECAP-DM studies suggest that between 30 to 40 % of patients with type 2 diabetes experience symptomatic hypoglycaemia. The results of the UK hypoglycaemia study demonstrated a similar annual prevalence of around 7% of patients with type 2 diabetes treated with a sulphonylurea experiencing disabling hypoglycaemia, which was similar in prevalence to that experienced by patients recently (< 2 years) commenced on basal insulin therapy. Patients with type 2 diabetes receiving insulin for > 5 years, particularly when the regimen contained a prandial insulin element experienced a similar prevalence of hypoglycaemia to that observed in patients with type 1 diabetes.

Question 8

A 46 year old aircraft engineer with a 22 year history of type 1 diabetes is referred by his GP for review. His current medication includes 'Novomix 30' 44 units in the morning and 46 units in the evening.

On examination his blood pressure is 135/75 mmHg, his BMI is 28 kg/m^2; his visual acuity is 6/9 in the right eye and 6/6 in the left eye. His most recent HbA1c is 65 mmol/mol (8.1%) (< 42.1 mmol/mol (6)) and his main complaint is that of recurrent problems with hypoglycaemia with 3 episodes over the last 4 months requiring paramedic assistance along with a reduction in his hypoglycaemia warning symptoms.

What advice should be given to this gentleman with respect to his driving?

- **A)** Discontinue driving for 1 month
- **B)** Discontinue driving for 3 months
- **C)** Discontinue driving for 6 months
- **D)** Discontinue driving for 1 year
- **E)** Discontinue driving for 2 years

Answer

Correct answer : Discontinue driving for 1 year

According to the most recent DVLA guidelines, patients on insulin therapy for diabetes:

- Must have awareness of hypoglycaemia.

  .
- There must be appropriate blood glucose monitoring.
- Must not be regarded as a likely source of danger to the public while driving.
- The visual standards for acuity and visual field must be met.

  If the patient meets the medical standard a 1, 2 or 3 year licence will be issued.

Question 9

A 36 year old man with a 21 year history of type 1 diabetes is reviewed in clinic. He feels generally well denies any hypoglycaemia, but historically has had poor glycaemic control. On examination, blood pressure is 151 / 77 mmHg, his BMI 29 kg/m^2, foot examination reveals no evidence of neuropathy while retinal screening reveals bilateral background retinopathy. His current medication includes novomix 30 and 42 units twice daily.
Investigations reveal:

		Normal Ranges
Hba1c	73.8 mmol/mol (8.9%)	(<42.1 mmol/mol (6))
Total Cholesterol	5.2 mmol/l	(<5)
LDL-Cholesterol	3.1 mmol/l	(< 3)
HDL-Cholesterol	1.3 mmol/l	(0.9 - 1.8)
Plasma Triglyceride	1.7 mmol/l	(0.9 - 2.2)
Albumin Creatinine ratio	6.9 mg / mmol creat	(<2.5)

Which of the following is the correct approach to treating this man’s lipid profile?

- **A)** Atorvastatin 20 mg od
- **B)** Atorvastatin 80 mg od
- **C)** Dietary modification only
- **D)** Ezetimibe 10 mg od
- **E)** Fenofibrate 150 mg od

Answer

Correct answer : Atorvastatin 20 mg od

Current NICE lipid lowering guidelines (July 2014) - offer atorvastatin 20 mg for the primary prevention of CVD to people who have a 10% or greater 10-year risk of developing CVD. Whilst cardiovascular assessment tools are not recommended for T1DM, they are useful as a guide in our scenario. Lipid lowering therapy for patients with diabetes under the age of 40 should be considered when there is an associated adverse cardiovascular risk factor profile such as co-existing poor glycaemic control, the presence of microvascular complications, features of metabolic syndrome and family history of premature cardiovascular disease. This patient should thus be considered for lipid lowering therapy with atorvastatin as he has evidence of microvascular complications in the form of microalbuminuria and retinopathy combined with poor glycaemic control. This guidance is based on data from all of the major statin studies in which the relative cardiovascular risk reduction associated with cholesterol lowering occurs independent of baseline cardiovascular risk, being related to the order of magnitude of cholesterol reduction.

Question 10

A 55 year old male with a 5 year history of type 2 diabetes is receiving fenofibrate therapy for treatment of a hypertriglyceridemia associated with low HDL and normal LDL.
Which of the following describes the mechanism of action of fibrate therapy?

- **A)** 3-HMG-CoA inhibitor
- **B)** Bile sequestrant
- **C)** Inhibits GI reabsorption of cholesterol
- **D)** PPAR-alpha agonist
- **E)** PPAR-gamma agonist

Answer

Correct answer : PPAR-alpha agonist

Fibrates are PPAR alpha receptor agonists and through this route are responsible for reduced hepatic triglyceride secretion, increased lipoprotein lipase activity and increased clearance of remnant LDL particles. These class of drugs are particularly useful in reducing triglycerides and increasing HDL – the typical dyslipidemia associated with diabetes.

Question 11

A 56 year old male with type 2 diabetes is being treated with metformin 1g bd but has a HbA1c of 7.6% (59mmol/mol). After a discussion with the patient, he is commenced upon vildagliptin. Through which of the following mechanisms does vildagliptin function?

- **A)** DPP-IV inhibitor
- **B)** SGLT-1 inhibitor
- **C)** GLP-1 agonist
- **D)** Potassium channel blocker
- **E)** PPAR-gamma agonist

Answer

Correct answer : DPP-IV inhibitor

Vildagliptin and sitagliptin are a class of drugs that inhibit the enzyme, dipeptidyl peptidase DPP-IV, which is responsible for the breakdown of GLP-1. GLP-1 has a very short half-life and is particularly important in glucose homeostasis producing delayed gastric emptying, suppression of glucagon and glucose mediated insulin secretion. Consequently, the extension of the half-life of endogenous GLP-1 improves glucose homeostasis in type 2 diabetes mellitus (T2DM).

Mechanism of acttion of DPPIV inhibitors JCEM article

Question 12

A 56 year old woman with a history of type 2 diabetes, hypertension, retinopathy and peripheral neuropathy attended her routine chiropody clinic and mentioned a 6-week history of dull aching discomfort of the right foot. Her vital signs were normal. On foot examination, there were bounding peripheral pulses and no ulcer was observed. A digital foot thermometer measurement showed that the temperature was 20 degrees centigrade on the left foot and 26 degree centigrade on the right foot.

Which of the following is the most likely diagnosis for this lady?

- **A)** Abscess of the right foot
- **B)** Charcot neuroarthropathy
- **C)** Diabetic foot osteomyelitis
- **D)** Pes planus
- **E)** Traumatic fracture of the right foot unaware by the patient due to neuropathy

Answer

Correct answer : Charcot neuroarthropathy

This patient with diabetic neuropathy presented with insidious onset discomfort, mid-foot deformity and signs of inflammation, which is a common presentation of charcot neuroarthropathy. Gradual onset and signs of inflammation is not consistent with a traumatic fracture and again is characteristic feature of charcot neuroarthropathy.

Question 13

A 28 year old woman with type 1 diabetes for 14 years has poor glycaemic control with an HbA1c of 112 mmol/mol (12.4%) (<42.1 mmol/mol (6)). She has pre-proliferative (severe non-proliferative) diabetic retinopathy and you are going to refer her to an ophthalmologist for assessment. What advice would you give her when she enquires about the likelihood of needing laser treatment?

- **A)** Laser treatment will only be necessary if she develops proliferative retinopathy
- **B)** Laser treatment is 60% effective in preventing loss of vision
- **C)** Laser treatment is 90% effective in preventing loss of vision
- **D)** Recurrent laser treatments will not affect her ability to drive
- **E)** She will need to have her eye immobilised to undergo laser treatment

Answer

Correct answer : Laser treatment is 90% effective in preventing loss of vision

According to the Early Treatment of Diabetic Retinopathy study, laser treatment is 90% effective in preventing loss of vision in type 1 diabetes but only 50% in preventing loss of vision if the predominant type of retinopathy is macular oedema (mostly seen in type 2 diabetes). Pan-retinal treatment is often associated with loss of the peripheral visual field which may affect her ability to drive if both eyes are treated although this is usually only an issue after several treatments. She will not need her eye to be immobilised but will need to be able to hold it still during treatment.

Question 14

A 38 year old lady with 21 year history of type 1 diabetes has a most recent HbA1c of 58.5 mmol/mol (7.5%) (<42.1 mmol/mol (6)). Her current therapy includes insulin glargine and humalog via a basal bolus regimen at a total daily insulin dose of 79 units. She has no clinical evidence of microvascular complications although her most recent digital retinal screen demonstrated the presence of background retinopathy in the right eye.
Which of the following lesions would be expected in this retinal image to classify this as mild non-proliferative (background) diabetic retinopathy?

- **A)** Dot haemorrhages
- **B)** Branch retinal vein occlusion
- **C)** Cotton wool spots
- **D)** Intraretinal microvascular abnormality (IRMA)
- **E)** Venous beading

Answer

Correct answer : Dot haemorrhages

Cotton wool spots are a pre-proliferative feature and signify retinal ischaemia, however they do not define pre-proliferative retinopathy. If cotton wool spots are present then other features - any venous bleeding, any venous reduplication, any IRMA, or blot haemorrhages - should be looked for. Other sight threatening features are intraretinal microvascular abnormalities (early new vessels), new vessels on the disc or elsewhere, venous beading (retinal ischaemia), multiple deep haemorrhages (ischaemia) and hard exudates near the fovea as they are often associated with fluid leakage and macular oedema. Background/mild nonproliferative retinopathy is described by hard exudates, dot and blot haemorrhages.

Grading of retinopathy

Question 15

A 58 year old man with a 5 year history of type 2 diabetes attends your clinic with blurred central vision. On examination he has moderate background retinopathy with multiple lesions close to the macula centre. His BMI is 33 kg / m^2 and his blood pressure is 168 / 88 mmHg. His current medication consists of metformin 850 mg three times a day, gliclazide 120 mg twice daily, simvastatin 20 mg once daily and lisinopril 20 mg once daily.

		Normal Ranges
Hba1c	73.8 mmol/mol (8.9%)	(<42.1 mmol/mol (6))
Total Cholesterol	6.2 mmol/l	(<4)
Plasma Triglyceride	2.2 mmol/l	(0.9 - 2.2)
eGFR	59 ml/min/1.73m^2;	(90 - 110)
Urine Albumin to Creatinine Ratio (ACR)	4.7 mg/ mmol creat	(<2.5)

Which of the following treatment strategies would be most appropriate?

- **A)** Add a third oral agent with the aim of improving his glycaemic control over several weeks, there is no need to refer to an ophthalmologist as his blurred vision is likely due to hyperglycaemia.
- **B)** Do nothing other than refer him to an ophthalmologist.
- **C)** Initiate insulin with the aim of rapidly improving his glycaemic control and refer him to an optician for new glasses.
- **D)** Initiate insulin and gently titrate the dose to reduce his HbA1c over several weeks and refer him to an ophthalmologist.
- **E)** Switch to insulin so as to rapidly improve his glycaemic control and refer to an ophthalmologist.

Answer

Correct answer : Initiate insulin and gently titrate the dose to reduce his HbA1c over several weeks and refer him to an ophthalmologist.

This man needs better glycaemic control but this should be done gently so as not to suddenly drop the glucose levels as this is associated with retinal artery vasoconstriction which may lead to a rapid deterioration of retinopathy. His blurred vision is likely due to a maculopathy and macular oedema so referral to an ophthalmologist is also required.

Question 16

A 39 year old lady with a 28 year history of type 1 diabetes with chronic poor glycaemic control has a most recent Hba1c of 86.9 mmol/mol (10.1%) (<42.1 mmol/mol (6)). Her current insulin regimen includes twice daily novomix 30 at doses of 34 units in the morning and 38 units in the evening. On examination, her blood pressure is 144/68 mmHg, her BMI is 23 kg/ m^2 and examination of her feet reveals reduced vibration, proprioception and thermosensation in both feet. Retinal screening reveals evidence of neovascularisation in the left eye.
Which of the following factors has been shown to have an important role in regulating retinal capillary blood flow?

- **A)** Contractile action of endothelial cells.
- **B)** Contractile action of pericytes.
- **C)** Local release of interleukins.
- **D)** Local release of nitric oxide.
- **E)** Release of vascular endothelial growth factor.

Answer

Correct answer : Contractile action of pericytes.

The retinal pericytes regulate retinal capillary blood flow but they are often damaged and reduced in number in patients with diabetic retinopathy leading to disordered blood flow regulation and increased shear stress on the vessel walls which drives the pathogenesis of retinopathy.

Question 17

A 24 year old Asian lady attends the antenatal clinic following a 75 gram oral glucose tolerance test at 24 weeks gestation which revealed a fasting plasma glucose of 6.9 mmol/l, a 1 hour post challenge plasma glucose level of 11.7 mmol/l and a 2-hour post challenge plasma glucose of 10.8 mmol/l. On examination her blood pressure is 132/68 mmHg and her BMI is 29 kg/m^2.

What is the potential impact of the results of her glucose tolerance test on the outcome of her pregnancy?

- **A)** There is a 2 - 3 fold increased risk of stillbirth
- **B)** There is a 2 - 3 fold increased risk of Down syndrome
- **C)** There is a 2 - 4 fold increased risk of neural tube defects
- **D)** There is a 2 - 4 fold risk of the baby subsequently developing type 1 diabetes
- **E)** Shoulder dystocia occurs in 15 - 20% of cases

Answer

Correct answer : Shoulder dystocia occurs in 15 - 20% of cases

Macrosomia and neonatal hypoglycaemia are the commonest complications of gestational diabetes, with the risk of both being significantly increased with poor glucose control during the 2^{nd} and 3^{rd} trimester. Macrosomia defined by a birth weight > 4.5Kg effects up to 45% of babies with shoulder dystocia being a common delivery problem occurring in up to 15 - 20% of cases. Still birth occurs in 2 – 3% of the general population and this is not increased in gestational diabetes, generally gestational diabetes does not cause birth defects since insulin resistance and thus hyperglycaemia does not become pronounced until second and third trimester. Women with pregestational diabetes, by contrast, have a 3- 5 fold increase risk of stillbirth and neural tube defects, but similar to gestational diabetes, there is no increased risk of chromosome abnormalities. These risks are augmented with poor glucose control during the first trimester. Gestational diabetes does not significantly increase the risk of type 1 diabetes in the offspring, rather a paternal history of type 1 diabetes appears to be a more pertinent factor.

Question 18

A 71 year old lady with a 5 year history of type 2 diabetes is referred by her GP for assessment and management of her possible diabetic nephropathy. Current medication includes metformin 850 mg three times daily and perindopril 4 mg once daily. On examination, her blood pressure is 144/86 mmHg, her BMI is 31 kg/m^2 and there is reduced vibration and proprioception sensation in both feet.

		Normal Ranges
Hba1c	57.4 mmol/mol (7.4%)	(<42 mmol/mol (6))
eGFR	55ml/min/1.72m²	
Urine Albumin Creatinine Ratio (ACR)	14.6 mg/mmol creat	(<3.5)

What level of albumin to creatinine ratio (ACR) confirms a diagnosis of proteinuria?

- **A)** ≥2.5 mg/mmol
- **B)** ≥30 mg/mmol
- **C)** ≤40 mg/mmol
- **D)** ≥50 mg/mmol
- **E)** ≥60 mg/mmol

Answer

Correct answer : ≥30 mg/mmol

An ACR of 30 mg/mmol or above confirms a diagnosis of proteinuria. In contrast, microalbuminuria is defined as an ACR > 2.5 mg/mmol for men and > 3.5 mg/mmol for women; these diagnostic criteria are used in the NICE CKD clinical guidance (November 2008) or between 30 and 300 µg albumin/mg creatinine. Diagnosis can only be confirmed after two samples have been assessed, separated by a few weeks.

Question 19

A GP colleague contacts you for advice on a patient with type 2 diabetes and deteriorating renal function. The patient is a 69 year old man with a 6 year history of type 2 diabetes. His current medication includes gliclazide 160 mg once daily, metformin 500 mg twice daily lisinopril 20 mg once daily, amlodipine 5 mg once daily and pravastatin 20 mg once daily. His blood pressure is 145/75 mmHg and he has evidence of background retinopathy on retinal screening.

		Normal Ranges
eGFR	44 ml/min/1.72m²	(90-110)
Urine Albumin:creatinine Ratio (ACR)	10.5 mg/mmol	(<2.5)
HbA1c	65.0 mmol/mol (8.1%)	(<42.1 mmol/mol (6))

At which level of eGFR would you advise the GP to discontinue metformin therapy?

- **A)** eGFR ≤ 15 ml/min/1.72m^2
- **B)** eGFR ≤ 30 ml/min/1.72m^2
- **C)** eGFR ≤ 40 ml/min/1.72m^2
- **D)** eGFr ≤ 50 ml/min/1.72m^2
- **E)** eGFR ≤ 60 ml/min/1.72m^2

Answer

Correct answer : eGFR ≤ 30 ml/min/1.72m2

Product characteristics for metformin state that it should be discontinued at an eGFR < 50, however in clinical practice an eGFR < 30 (stage four chronic kidney disease (CKD 4)) is considered to represent an absolute indication for the discontinuation of metformin. Whilst not a contraindication to metformin, an eGFR 30 – 59 should alert clinicians to evaluate the need for possible dose reduction or discontinuation of metformin particularly if other risk factors for metformin toxicity are present such as heart failure. Renal function and metformin safety is based on the fact that metformin is renally cleared. In the setting of significant renal impairment particularly in the presence of an inter-current illness resulting in relative tissue hypoxia, there is a marked increase in the risk of metabolic acidosis (lactic acidosis) in patients with renal impairment receiving metformin therapy.

Question 20

A 63 year old man with a 7 year history of type 2 diabetes attends clinic for review. On examination he has bilateral background retinopathy along with reduced vibration and 10 g microfilament sensation in both feet, his BMI is 32 kg/m^2 and his blood pressure is 152/90 mmHg. His current medication includes metformin 1 gram twice daily gliclazide 160 mg twice daily, insulin glargine 32 units once daily, lisinopril 10 mg once daily and simvastatin 40 mg once daily.

		Normal Ranges
HbA1c	61.7 mmol/mol (7.8%)	(<42.1 mmol/mol (6))
Total Cholesterol	4.4 mmol/l	(<5)
Plasma Triglyceride	2.7 mmol/l	(0.9 - 2.2)
U+E	Normal	
Urine Albumin:Creatinine Ratio (ACR)	9.9 mg/mmol	(<2.5)

Which of the following is the following is the most appropriate blood pressure target for this patient?

- **A)** <130 / 80 mmHg
- **B)** <140 / 80 mmHg
- **C)** <120 / 80 mmHg
- **D)** <130 / 70 mmHg
- **E)** <110 / 70 mmHg

Answer

Correct answer : <130 / 80 mmHg

This patient has microalbuminuria as defined by an elevated albumin to creatinine ratio. The diagnosis of microalbuminuria is confirmed by two measurements at least 1 week apart > 2.5 mg/mmol for males and > 3.5 mg/mmol for females. The identification of microalbuminuria identifies patients at an increased risk of cardiovascular disease and is an indication for intensive multiple risk factor intervention. Current NICE guidelines (November 2008) advocate an optimal target blood pressure for such patients of < 130 / 80 mmHg.

Question 21

A 65 year old man with a 7 year history of type 2 diabetes is reviewed in clinic. He feels generally well and his glucose control has improved since commencing insulin 4 months previously with his current HbA1c measuring 57.4 mmol/mol (7.4%) (<42.1 mmol/mol (6)). His main complaint is that of burning discomfort in both feet which is more severe at night. He has experience only minimal relief with co-codamol and non-steroidal anti-inflammatory based analgesia.

On examination his blood pressure is 144 / 77 mmHg, his BMI is 32 kg/m^2, retinal screening reveals features of background retinopathy in his left eye and examination of his feet reveals reduced vibration and proprioception sensation in both feet.

Which of the following is the most appropriate therapeutic option for managing this patient's symptoms?

- **A)** Capsaicin 0.025 % topically
- **B)** Citalopram 10 mg daily
- **C)** Duloxetine 60 mg daily
- **D)** Fluoxetine 20 mg daily
- **E)** paracetamol 1 gram daily

Answer

Correct answer : Duloxetine 60 mg daily

In accordance with NICE guidelines 173, for people with painful diabetic neuropathy, offer oral duloxetine 60 mg, amitriptyline, pregabalin or gabapentin as first-line treatment. If the initial choice fails despite maximum tolerated dose, offer other first line agents - oral amitriptyline 10 mg, oral pregabalin 150 mg or gabapentin 300 mg tds. Hence in our scenario the duloxetine is the correct choice. If satisfactory pain reduction is still not achieved with second-line treatment, refer the patient to a specialist pain service and/or a condition specific service. While waiting for referral, consider oral tramadol or topical lidocaine.

Tight control of blood glucose can reverse the changes of diabetic neuropathy, but only if the neuropathy and diabetes is recent in onset. Conversely, painful symptoms of neuropathy in uncontrolled diabetics tend to subside as the disease and numbness progress. Of course, these uncontrolled patients are at great risk for diabetic foot ulcers and amputation.

Reference:

NICE clinical guidelines 173: Neuropathic pain

Question 22

A 55 year old Asian lady with a 3 year history of diet controlled type 2 diabetes is reviewed in clinic. Her glucose is well controlled with a most recent HbA1c measuring 51.9 mmol/mol (6.9%) (<42.1 mmol/mol (6)). On examination her blood pressure is 134 / 74 mmHg and her BMI is 31 kg / m^2. Her main complaint at present is that of persisting tingling and discomfort in her feet at night.

Which of the following apply in the clinical assessment of diabetic peripheral sensory neuropathy?

- **A)** Small fiber function may be assessed using a tuning fork
- **B)** Large fiber function may be assessed by thermal discrimination
- **C)** Loss of vibration sensation is an early clinical feature
- **D)** Loss of ankle jerk reflexes is an early clinical feature
- **E)** Medial plantar sensory action potential is undetectable in patients with neuropathy

Answer

Correct answer : Loss of vibration sensation is an early clinical feature

Small fiber function may be assessed via evaluation of thermal discrimination, while large fiber function is a determinant of vibration and proprioception sensation and may be clinically evaluated with a tuning fork. Medial plantar sensory action potential is undetectable in subjects with normal vibration and thermal thresholds. Large fiber dysfunction and thus loss of vibration and proprioception sensation is the earliest manifestation of peripheral sensory-motor neuropathy in diabetes.

Question 23

A 69 year old lady with a 7 year history of type 2 diabetes is reviewed in clinic. Her main complaint is of numbness in her feet. Current medication includes metformin 1 gram twice daily, Insulin glargine 32 units at night, perindopril 4 mg once daily, simvastatin 20 mg once daily and aspirin 75 mg once daily. On examination her blood pressure is 155 / 56 mmHg, her BMI is 33 kg /m^2 peripheral pulses are present but vibration sensation is reduced in both feet. Investigations reveal:

		Normal Ranges
HbA1c	62.8 mmol/mol (7.9%)	(<42.1 mmol/mol (6))
Urine Albumin:Creatinine Ratio	3.9 mg/mmol creat	(<3.5)
eGFR	55 ml/min/1.73m²	(90-110)

Which of the following is a typical feature of large fibre neuropathy?

- **A)** Hyperaesthesia
- **B)** Impaired thermosensation
- **C)** Paraesthesia
- **D)** PR interval variation
- **E)** Reduced sweating

Answer

Correct answer : Paraesthesia

Large fiber involvement in neuropathy results in reduced proprioception and vibration sensation and is the earliest clinically identifiable feature of peripheral sensory motor neuropathy. The primary symptom associated with large fibre dysfunction is paraesthesia and an increased risk of charcot arthropathy, particularly in association with autonomic nerve dysfunction. Examination findings include reduced vibration and proprioception sensation, diminished ankle jerks, muscle wasting and increased blood flow. Reduced light pressure sensation and vibration sensation are the earliest clinically identifiable manifestations of large fibre neuropathy.

Question 24

A 39 year old man with a 21 year history of type 1 diabetes with chronic poor control has a most recent HbA1c of 76.0 mmol/mol (9.1%) (<42.1 mmol/mol (6). His current medication includes novomix 30 56 units in the morning and 64 units in the evening. Retinal screening reveals bilateral background retinopathy and urinalysis reveals an albumin:creatinine ratio of 4.9 mg / mmol creat (< 2.5). His main complaint is that of burning discomfort in both feet. Examination of his feet reveals them to be cold but with preserved peripheral pulses and reduced thermosensation, vibration and proprioception sensation.

Which of the following would suggest a diagnosis of short fiber neuropathy?

- **A)** Muscle wasting
- **B)** Decreased light pressure sensation
- **C)** Diminished ankle jerks
- **D)** Paraesthesia
- **E)** Reduced thermosensation

Answer

Correct answer : Reduced thermosensation

Short fiber neuropathy is a later manifestation of diabetic peripheral neuropathy, with symptoms including hyperparesthesia and superficial pain. Examination findings indicative of short fiber neuropathy include impaired thermosensation, reduced sweating and a cold foot although reflexes are not involved.

Question 25

A 26 year old lady with a 21 year history of type 1 diabetes is reviewed in clinic. Her current medication includes insulin glargine and novorapid via a basal bolus regimen at a total daily dose of 74 units. She has had long standing poor glucose control with a most recent Hba1c of 108.7 mmol/mol (12.1%) (<42.1 mmol/mol (6)). She complains of feeling faint on standing and also has noticed an increasing frequency of diarrhoea. On examination her blood pressure is 112/68 mmHg when supine and 96/56 mmHg on standing, her body weight is 56 kg and her BMI is 20 kg/m^2 . Examination of her feet reveals reduced vibration and proprioception sensation in both feet.

Which of the following investigations would support a diagnosis of autonomic neuropathy ?

- **A)** > 5 mmHg variation in diurnal blood pressure
- **B)** > 10 mmHg change in systolic blood pressure 20 minutes after a meal
- **C)** Heart rate variability of < 10 beats per minute with respiration
- **D)** QT - interval of < 440 ms
- **E)** Longest R-R to shortest R-R ratio during valsalva maneuver > 1.2

Answer

Correct answer : Heart rate variability of < 10 beats per minute with respiration

Heart rate variability during breathing of < 10 beats per minute is indicative of autonomic neuropathy. A change in postprandial systolic blood pressure > 20 mmHg is considered abnormal, while a variation in diurnal blood pressure > 15 mmHg is considered abnormal. During the valsalva maneuver the subject forcibly exhales into the mouthpiece of a manometer to 40 mmHg for 15 seconds during ECG monitoring. Healthy subjects develop tachycardia and peripheral vasoconstriction during strain and an overshoot bradycardia and rise in blood pressure with release. The ratio of longest R-R to shortest R-R should be > 1.2. The heart rate response to standing may also be useful in evaluating possible autonomic neuropathy. During continuous ECG monitoring, the R-R interval is measured at beats 15 and 30 after standing. Normally, a tachycardia is followed by reflex bradycardia. The 30:15 ratio is normally > 1.03. Heart rate variability measures predominantly evaluate parasympathetic nervous system integrity, while blood pressure changes predominantly test sympathetic nervous system integrity. A Q-T interval > 440 ms is abnormal and suggestive of parasympathetic autonomic neuropathy. These diagnostic values refer to measurements in patients less than 60 years of age. It is important to note that autonomic function tests tend to decline with age.

Question 26

A 32 year old lady with a 20 year history of type 1 diabetes is reviewed in clinic. Her current medication includes novomix 30 32 units twice daily. Her control has historically been poor with her most recent Hba1c measuring 86.9 mmol/mol (10.1%) (<42.1 mmol/mol (6)).

On examination her blood pressure is 105 / 65 mmHg and her body weight is 63 kg.

Examination of her feet reveals reduced absent ankle jerks bilaterally and reduced vibration and proprioception in both feet. Her main complaint is that of increasingly frequent episodes of fecal incontinence.

Which of the following clinical features would support a diagnosis of autonomic neuropathy?

- **A)** Heart rate increase on deep breathing > 15 beats per minute
- **B)** Heart rate increase on standing after 15 seconds <12 beats per minute
- **C)** Generalized sweating
- **D)** Postural systolic blood pressure drop 2 minutes after standing > 15 mmHg
- **E)** Resting heart rate > 80 beats per minute

Answer

Correct answer : Heart rate increase on standing after 15 seconds <12 beats per minute

Heart rate increase on standing of < 12 beats per minute is indicative of autonomic neuropathy, a normal response being > 15 beats per minute. A postural fall in systolic blood pressure of > 30 mmHg 2 minutes after standing is suggestive of autonomic dysfunction as is a resting heart rate > 100 beats per minute. Clinical features which help establish a diagnosis of autonomic neuropathy include diarrhea, fecal incontinence and post-gustatory sweating.

Question 27

A 54 year old gentleman with a 2 year history of type 2 diabetes is reviewed in the clinic complaining of difficulty in walking and frequent episodes of tripping and stumbling particularly when walking uphill. He complains of pain but no paresthesia. His current medication includes metformin 500 mg three times a day, simvastatin 40 mg once daily, perindopril 4 mg once daily and aspirin 75 mg once daily.

On examination, his blood pressure is 144/74 mmHg, his BMI is 30 kg/m^2 examination of his legs reveals muscle wasting affecting the left thigh with marked reduction in power and muscle fasciculations, plantar flexion and dorsiflexion of both feet are normal and no sensory deficit can be identified.

Investigations reveal:

		Normal Ranges
HbA1c	56.3 mmol/mol (7.3%)	(<42.1 mmol/mol (6))
Total Cholesterol	4.4 mmol/l	(0.9 - 2.2)
Plasma Triglyceride	1.6 mmol/l	(0.9 - 2.2)
Creatinine Kinase (CK)	74 U/L	(38 - 174)
ESR	11 mm/hr	(<10)
CRP	4.1 mg/l	(<6)
eGFR	92 ml/min/1.73 m^2	(90-110)

Which of the following is the most likely diagnosis for this gentleman?

- **A)** Atrophic lateral sclerosis
- **B)** Diabetic amyotrophy
- **C)** Polymyositis
- **D)** Polymyalgia
- **E)** Lumbar degenerative disc disease

Answer

Correct answer : Diabetic amyotrophy

Diabetic amyotrophy is a disabling neuropathy that usually occurs in patients with type 2 diabetes mellitus in middle or later age. Concomitant weight loss is frequent. Patients usually have not had diabetes for a long time, and glycaemic dysregulation is often not severe. A diagnosis of diabetic amyotrophy leads to the discovery of underlying diabetes mellitus in one quarter to one third of cases. Long-term diabetic complications such as diabetic retinopathy and nephropathy are often absent at the time of diagnosis. The clinical presentation is characterized by sudden, sharp, and asymmetric pain that usually starts in one hip and thigh and subsequently spreads to the other side within weeks to months. Cases of worsening over 18 months are often described. Weakness starts distally in one third of cases, leading to unilateral or bilateral foot drop. As the pain improves, weakness becomes the major symptom; it affects both proximal and distal leg muscles. In about one third of cases, weakness spreads to proximal arm muscles and is attributed to cervicobrachial radiculoplexopathy . However, some of these upper extremity deficits result from compression neuropathy from reliance on the arms to support body weight. Approximately 12% of patients develop thoracic radiculopathy, leading to radiating belt-like chest or abdominal pain and intercostal muscle weakness causing pseudohernia. Prominent bulbar symptoms have been described. Respiratory weakness may also be the initial manifestation of diabetic proximal neuropathy. Amyotrophic lateral sclerosis (ALS) may occur from the teenage years to the late 80s, but peak age at onset occurs from 55-75 years with mean age of 62 years at diagnosis. Muscle weakness usually is asymmetric, and signs of upper and lower motor neuron involvement may be observed. In the initial stages, reflexes should be normal to increased, but as the disease becomes more advanced, reflexes may be diminished or absent. Fasciculations are commonly seen as a result of lower motor neuron involvement. Pathologic long-tract signs of upper motor neuron involvement, such as the extensor plantar response and/or Hoffmann's sign, may be present in patients with hyporeflexia or areflexia, depending upon the extent of the upper motor neuron involvement. In 75-80% of patients, symptoms begin with limb involvement, while 19-25% of patients present with bulbar symptoms. For those with limb involvement at presentation, incidence of upper limb versus lower limb involvement is approximately equal. Patients who have lower limb onset initially may complain of tripping, stumbling, or awkwardness when running. Those with upper limb onset may have difficulty with actions such as buttoning clothes, picking up small objects, or turning a key. With bulbar onset, patients note problems such as slurred speech, hoarseness, or decreased volume of speech.

The absence of any sensory symptoms coupled with preserved reflexes and no prior history of disc injury or back pain makes a diagnosis of lumbar radiculopathy unlikely, while the clinical picture coupled with normal inflammatory markers and CK levels also makes diagnosis of polymyalgia or polymyositis unlikely.

Question 28

A 75 year old lady with a 10 year history of type 2 diabetes complicated by ischaemic heart disease and congestive cardiac failure is reviewed in clinic. Her main complaint is that of electric shock like pains in both feet, particularly at night with only minimal relief from simple analgesia.

On examination her blood pressure is 106/55 mmHg, her BMI is 31 kg/m^2 and examination of her feet reveals bilateral pitting edema, reduced vibration sensation, thermosensation and proprioception sensation in both feet. Dorsalis pedis and posterior tibial pulses are palpable bilaterally. Her current medication includes novomix 30 26 units twice daily, metformin 500 mg twice daily, rosuvastatin 10 mg once daily, perindopril 4 mg once daily, amlodipine 5 mg once daily, bisoprolol 2.5 mg once daily and furosemide 40 mg once daily.
Investigations reveal

		Normal Ranges
Hba1c	62.8 mmol/mol (7.9%)	(<42.1 mmol/mol (6))
Total Cholesterol	3.6 mmol/l	(<5)
Plasma TG	1.7 mmol/l	(0.9 - 2.2)
eGFR	47 ml/min/1.73m²	(90-110)
LFT	Normal	
TSH	1.21 mIU/L	(0.32 - 5.5)

Which of the following would be the most appropriate initial therapy of choice for this lady's symptoms?

- **A)** Amitriptyline
- **B)** Capsaicin cream
- **C)** Fluoxetine
- **D)** Oxycodone
- **E)** Valproate

Answer

Correct answer : Amitriptyline

Guidance suggests that any of the neuropathic agents, Amitriptyline, gabapentin, duloxetine and pregabalin can be used in this scenario of painful diabetic neuropathy. If the initial agent fails then an alternative can be used. Whilst amitriptyline is the most appropriate choice from the options provided, its use may also be limited due to the anti-cholinergic side effects.

Tight control of blood glucose can reverse the changes of diabetic neuropathy, but only if the neuropathy and diabetes is recent in onset. Conversely, painful symptoms of neuropathy in uncontrolled diabetics tend to subside as the disease and numbness progress. Of course, these uncontrolled patients are at great risk for diabetic foot ulcers and amputation.

Reference:

NICE clinical guidelines 173: Neuropathic pain

Question 29

A 64 year old gentleman with a five year history of type 2 diabetes is reviewed in clinic. On examination, his current medication includes ploglitazone 30 mg once daily, gliclazide 160 mg twice daily, simvastatin 40 mg once daily, ramipril 5 mg once daily and amlodipine 5 mg once daily.

On examination, his blood pressure is 145/75 mmHg and his BMI is 33 kg/m^2. He has bilateral background retinopathy on retinal screening but has no evidence of peripheral sensory neuropathy. His current eGFR is 43 $ml/min/1.73m^2$ compared with 59 $ml/min/1.73m^2$ when measured 6 months previously.

Further investigations reveal:

		Normal Ranges
Hba1c	65.1 mmol/mol (8.1%)	(<42.1 mmol/mol (6))
Haemoglobin	11.9 g/ dl	(11 - 16)
Total Cholesterol	4.4 mmol/l	(<4)
Urine Albumin:creatinine ratio	8.9 mg/mmol/creat	(<2.5)

Which of the following is the most appropriate approach to the management of this gentleman?

- **A)** Repeat eGFR in 3 months
- **B)** Repeat eGFR in 6 months
- **C)** Arrange for 24 hour urine creatinine clearance measurement
- **D)** Arrange a routine referral for nephrology assessment
- **E)** Arrange for an urgent nephrology assessment

Answer

Correct answer : Arrange a routine referral for nephrology assessment

This gentleman has demonstrated a significant progression in kidney disease as defined by the observed decline in eGFR over a 6 month period. A decline in eGFR > 15 ml/min/1.72m^2 within 1 year defines significant progression of kidney disease and is an indication for further investigation and intensification of therapy. Initiation of ACE-I therapy or angiotensin receptor blocker therapy may result in a decline of eGFR of 15 – 25% as part of a normal response. A greater decline in response to the initiation of such agents should alert the clinician to the possibility of renovascular disease.

This gentleman may also have early renal anaemia. The WHO definition of normal haemoglobin levels for men and postmenopausal women is > 13 g / dl. In patients with diabetic nephropathy renal anaemia develops earlier than in people with non-diabetic kidney disease (this patient is likely to have diabetic nephropathy since he has evidence of other microvascular complications in the form of retinopathy). In diabetic kidney disease a threshold eGFR < 60 ml/min/1.73m^2 is advocated by the national service framework as the point at which to begin screening for renal anaemia. By using this threshold around 85% of cases would be identified.

Question 30

A 44 year old Asian lady with a 5 year history of type 2 diabetes is admitted to hospital with progressive pitting odema.

On examination, her blood pressure is 156/76 mmHg, her BMI is 38 kg/m^2 and fundoscopy reveals changes of background diabetic retinopathy in both eyes. Her current medication includes metformin 1 g twice daily, enalapril 5 mg once daily and simvastatin 20 mg once daily. Investigations reveal a grossly elevated 24 hour urinary protein content of 4.6 g/24 hours (< 0.3). She subsequently undergoes a renal biopsy as part of her ongoing investigation, the result of which is reviewed at the weekly clinical pathology meeting.

Which of the following microscopic changes would confirm a diagnosis of diabetic nephropathy?

- **A)** Cellular eosinophilic nodules found at the periphery of the glomerular tuft
- **B)** Focal nodular mesangial tissue expansion
- **C)** Glomerular basement membrane thickening
- **D)** Glomerular basement membrane atrophy
- **E)** Mesangial matrix thickening due to deposition of type V and Type VI collagen along with fibronectin

Answer

Correct answer : Focal nodular mesangial tissue expansion

Focal nodular mesangial tissue expansion is a characteristic early feature of diabetic nephropathy, with a close relationship existing between mesangial expansion and functional renal abnormalities. Immunostaining of the expanded matrix material reveals it to be mainly of type IV collagen with additional type V, laminin and fibronectin. Basement membrane thickening is invariably present in people with diabetes, irrespective of whether or not they have nephropathy and can be demonstrated within 2 – 3 years of diagnosis of type 1 diabetes. The Kimmelstiel-Wilson nodule is a specific feature of diabetic nephropathy but only occurs in 20 – 60% of patients with nephropathy. It comprises of an acellular eosinophillc laminated structure usually at the periphery of the glomerular tuft.

Question 31

A 26 year old woman with pre-existing type 1 diabetes for 12 years attends your medical antenatal clinic as she has just discovered that she is pregnant. This is an unplanned pregnancy and her HbA1c is 66.1 mmol/mol (8.2%) (<42.1 mmol/mol (6)). At her most recent retinal screening she was noted to have background retinopathy affecting the right eye. She is concerned as to the possible impact of her pregnancy on her eyes.
Which of the following is the most appropriate advice for this lady?

- **A)** Her retinopathy may deteriorate if she breast feeds.
- **B)** She does not require retinal screening during her pregnancy.
- **C)** She will require screening three times during her pregnancy.
- **D)** She will require an ACE-I to protect her from worsening retinopathy.
- **E)** She will require aspirin to protect her from worsening retinopathy.

Answer

Correct answer : She will require screening three times during her pregnancy.

Diabetic retinopathy may rapidly deteriorate during pregnancy due to the rapid improvement in glycemic control that is often achieved; she therefore needs dilated fundoscopy or photography every trimester. ACE inhibitors are contraindicated during pregnancy and aspirin does not have any data to support its use in pregnancy. Breast feeding will have no effect on retinopathy.

Question 32

A 22 year old law student is reviewed in clinic following her recent diagnosis with type 1 diabetes six months previously. She has an HbA1c of 73.8 mmol/mol 8.9% (<42.1 mmol/mol (6)) and she smokes 10 cigarettes a day. Her main concern relates to the effect that diabetes may have on her eyesight.

Which of the following is the most appropriate approach for this young lady?

- **A)** Achieving an HbA1c of 53.0 mmol/mol (7%) would reduce her risk of retinopathy developing by about 75%
- **B)** Any future pregnancy will have no effect on her eyes
- **C)** She is unlikely to develop retinopathy if she maintains an HbA1c <47.5 mmol/mol (6.5%)
- **D)** Stopping smoking will reduce her risk of developing retinopathy
- **E)** She is unlikely to develop any problems with her eyes for the next 10 years

Answer

Correct answer : Achieving an HbA1c of 53.0 mmol/mol (7%) would reduce her risk of retinopathy developing by about 75%

The Diabetes Control and Complications Trial showed a 75% reduction in retinopathy developing and a 60% reduction in progression from mild retinopathy associated with a reduction of HbA1c from 74.9 mmol/mol to 53.0 mmol/mol (from 9% to 7%). Unfortunately even with good control she will almost inevitably develop retinopathy and the risk is greater in type 1 diabetes compared to type 2 diabetes as demonstrated by the Wisconsin Epidemiologic Diabetic Retinopathy Study. Interestingly that study did not find an association between smoking and retinopathy. Features of retinopathy usually do not appear in patients with type 1 diabetes for up to 5 years following diagnosis, while pregnancy is associated with potential progression of retinopathy.

Question 33

A 37 year old woman has had type 1 diabetes for 34 years. For the last 2 years she has had a problem of vomiting 2 hours after her meals intermittently. A barium meal study has suggested gastroparesis. She has tried various treatments for this but all with limited success. She has difficulty controlling her blood glucose levels postprandially as these are either high if she doesn't give enough short acting insulin or low if she vomits 2 hours after a meal. It is suggested that she tries a continuous subcutaneous insulin infusion to try to help with this problem. You are asked to advise on her mealtime boluses; you would suggest:

- **A)** Delay giving her bolus until her blood glucoses start to rise postprandially
- **B)** Do not give a mealtime bolus but measure the glucose 2 hours post-prandially and give an appropriate correction bolus
- **C)** Do not give a mealtime bolus but increase the basal rate around the mealtimes to cover the rise in glucose.
- **D)** Give the bolus of insulin over a protracted time such as 60 to 120 minutes
- **E)** Put a longer acting insulin into the pump instead of the usual short acting insulin

Answer

Correct answer : Give the bolus of insulin over a protracted time such as 60 to 120 minutes

This can be a difficult issue to address to a satisfactory degree. Delaying giving a bolus until glucoses rise is likely to allow symptoms of hyperglycaemia to develop. If the basal rate is increased this is restrictive in terms of timing of meals and both type and amount of food and allowing freedom of choice of food is a major benefit of using continuous subcutaneous insulin infusion. Giving a bolus over a protracted period of time (also known as a square wave bolus) can help to overcome this problem.

Question 34

A 60 year old female is seen as part of the retinal screening service. Her vision is fine at 6/9 bilaterally and she is noted to have a couple of microaneurysms only in both eyes. When should this patient next have retinal screening?

- **A)** one month
- **B)** three month
- **C)** six months
- **D)** one year
- **E)** two years

Answer

Correct answer : one year

With background retinopathy the interval between screening is recommended as annual. A 4 month interval is suggested for preproliferative retinopathy.

Question 35

A 74 year old male presents with a six month history of deteriorating fatigue and weakness. He was diagnosed with type 2 diabetes approximately 15 years ago together with hypertension. He receives gliclazide 40 mg bd, metformin 1g bd and atenolol 50 mg daily.
On examination, his blood pressure is 154/88 mmHg lying and standing, he has evidence of a peripheral neuropathy to mid tibia and has some dot haemorrhages on fundal examination.

		Normal Ranges
Sodium	133 mmol/L	(135-145)
Potassium	5.6 mmol/L	(3.5-5)
Urea	8.5 mmol/L	(3-8)
Creatinine	133 mmol/L	(50-100)
Plasma glucose	10.1 mmol/L	(3.5-6.0)
HbA1c	7.8% (62 mmol/mol)	(<6)

Which of the following is the likely explanation for his presentation and biochemistry?

- **A)** Drug induced
- **B)** Hypoadrenalism
- **C)** Hyporeninemic hypoaldosteronism
- **D)** Liddle's syndrome
- **E)** Renal artery stenosis

Answer

Correct answer : Hyporeninemic hypoaldosteronism

This patient presents with weakness, has a hyperkalemia and hyponatraemia together with mild chronic renal impairment. The biochemistry is suggestive of a type IV renal tubular acidosis (hyporeninemic hypoaldosteronism). This is not uncommon in elderly patients, particularly with diabetes and may be exacerbated by drugs such as NSAIDS and beta blockers. Treatment is usually successful with withdrawal of the offending agents and a low potassium diet. Small doses of fludrocortisone can be used but care needs to be exercised with hypertension.

Question 36

A 28 year old male with a 20 year history of type 1 diabetes is referred to the clinic after moving to the area for a new job. Amongst his notes you see that previous retinal screening classifies him as 'Retinopathy R1'.

Which of these was therefore noted at his last retinal screening?

- **A)** Detached macula
- **B)** Intraretinal microvascular abnormalities (IRMAs)
- **C)** Venous beading
- **D)** Microaneurysms
- **E)** New vessels

Answer

Correct answer : Microaneurysms

The National Screening Committee has produced guidance grading the lesions present on retinal screening. These are

R1 - background retinopathy - in this case microaneurysms

R2 - pre-proliferative retinopathy

R3 - proliferative retinopathy

M - maculopathy

P - photocoagulation

U - ungradeable

Question 37

A 32 year old male with a 20 year history of type 1 diabetes undergoes digital retinal screening. The report returns grading the retinal images as 'Retinopathy R2'.
Which of following lesions is present on retinal images to account for this grade?

- **A)** Microaneurysms
- **B)** Maculopathy
- **C)** New vessels on the disc
- **D)** Photocoagulation scars
- **E)** Venous beading

Answer

Correct answer : Venous beading

The National Screening Committee has produced guidance grading the lesions present on retinal screening. These are

R1 - background retinopathy

R2 - pre-proliferative retinopathy

R3 - proliferative retinopathy

M - maculopathy

P - photocoagulation

U - ungradeable

The grading of retinopathy R2 suggests pre-proliferative changes.

Question 38

A 55 year old diabetic male attends for annual review. He is currently on atorvastatin 40 mg and fenofibrate 200 mg per day and has the following profile:

		Normal Ranges
Albumin	38 g/L	(30-50 g/L)
ALP	66 U/L	(50-125 U/L)
ALT	41 mU/L	(05-58 U/L)
Bilirubin	0.6 mg/L	(0.1-1 mg/L)
Proteins	69 g/L	(60-80 g/L)
Free T4	17.2 pmol/L	(11.5-22.7 pmol/L)
TSH	2.5 mU/L	(0.35-5.5 mU/L)
LDL	2.0 mmol/L	
Total Cholesterol	4.0 mmol/L	
TGs	5.8 mmol/L	
HbA1C	48.6 mmol/mol (6.6%)	

What is the next most appropriate step in his management?

- **A)** Increase atorvastatin to 80 mg
- **B)** Start ezetimibe
- **C)** Start niacin
- **D)** Start omega fatty acid
- **E)** No changes required

Answer

Correct answer : No changes required

According to the NICE guidelines on Type 2 Diabetes mellitus (DM), a type 2 DM patient with high serum triglyceride levels should be initially assessed for a possible secondary cause of hypertriglyceridemia (including poorly controlled diabetes, hypothyroidism, Cushing's syndrome, chronic renal failure, drugs such as steroids, estrogens, isotretinoin) and treated if such a cause is identified. If the TG levels remain elevated then fibrates can be offered in the specialist setting. However, in the most recent guidance no additonal therapy should be offered in terms of primary prevention. Regarding IMPROVE-IT this was with ezetimibe in acute coronary syndromes.

Do not routinely offer fibrates and do not offer nicotinic acid (niacin), a bile acid sequestrant (anion exchange resin) or omega-3 fatty acid compounds for the prevention of cardiovascular disease to any of the following:

- **people who are being treated for primary prevention**
- **people who are being treated for secondary prevention**
- **people with chronic kidney disease**
- **people with type 1 diabetes**
- **people with type 2 diabetes.**

Tell people that there is no evidence that omega-3 fatty acid compounds help to prevent cardiovascular disease. Do not offer the combination of a bile acid sequestrant (anion exchange resin), fibrate, nicotinic acid or omega-3 fatty acid compound with a statin for the primary or secondary prevention of cardiovascular disease. Do not offer coenzyme Q10 or vitamin D to increase adherence to statin treatment.

Hypertriglyceridemia

NICE on lipid lowering therapies

Question 39

What should be the weight of monofilament used to check for peripheral neuropathy in diabetics?

- **A)** 1 g
- **B)** 5 g
- **C)** 10 g
- **D)** 20 g
- **E)** 100 g

Answer

Correct answer : 10 g

According to the NICE guidelines regarding the management of diabetic foot ulcers (NICE clinical guideline 10), examination of a patient's feet should include;

- Testing of foot sensation using a 10 g monofilament or vibration
- Palpation of foot pulses
- Inspection of any foot deformity and footwear

The foot risks are classified as:

- At low risk (need annual review)
- At increased risk: in the presence of peripheral neuropathy or vascular insufficiency (arrange regular review at a 3-6 monthly interval, by the foot protection team)
- At high risk: in the presence of peripheral neuropathy or vascular insufficiency along with deformity or previous ulcer or skin change (arrange frequent reviews 1-3 monthly)
- Foot care emergencies including new ulceration, swelling or discolouration (review by multidisciplinary foot care team within 24 hours)

Question 40

A 55 year old lady with a background history of type 2 diabetes mellitus presents to clinic with a warm and swollen left foot. Peripheral pulses are palpable but there is bilateral sensory loss in the distal extremities. There is no superficial skin ulcer and range of movement is restricted as the foot looks swollen and deformed. What is the next best step in her management?

- **A)** Complete contact cast
- **B)** IV antibiotics
- **C)** NSAIDs
- **D)** Oral antibiotics
- **E)** Urgent vascular assessment

Answer

Correct answer : Complete contact cast

Charcot's arthropathy is a rare, progressive degeneration of weight bearing joints. It is seen associated with diabetes mellitus, alcoholic neuropathy, cerebral palsy and spinal cord lesions. The underlying mechanism leading to Charcot's arthropathy is unclear although recurrent micro-trauma to a joint (predisposed by absent peripheral sensation and proprio-reception) or dysregulated autonomic nervous system (leading to increased perfusion) seem to play a part in its pathogenesis.

The commonest joints afflicted with Charcot's arthropathy in diabetes mellitus include tarso-metatarsal joint and metatarsophalangeal joint. Patients present with swelling of the joint and clinical examination reveals a mildly raised temperature of the affected joint during the acute phase. A MRI scan can aid in diagnosis and treatment includes a complete contact cast to avoid development of deformities like rocker bottom foot and tarsometatarsal dislocation.

Question 41

A newly diagnosed type 2 diabetic male is referred to the clinic. His BMI is 28 kg/m^2 and he drinks 4 units of alcohol every week. His blood pressure is 134/82 mmHg and examination is otherwise essentially normal. His biochemistry shows:

		Normal Ranges
Albumin	42 g/L	(30-50 g/L)
ALP	202 U/L	(50-125 U/L)
ALT	116 mU/L	(5-58)
Bilirubin	35 micromol/L	(0-18)
Proteins	72 g/L	(60-80)
HbA1c	65.0 mmol/mol (8.1%)	(<42.1 mmol/mol (6))

In view of the deranged LFTs an ultrasound of the abdomen is arranged which reveals fatty infiltration of the liver.
Besides lifestyle interventions and metformin, which of the following should be considered in his case?

- **A)** Exenatide
- **B)** Insulin
- **C)** Empagliflozin
- **D)** Pioglitazone
- **E)** Sulphonylureas

Answer

Correct answer : Pioglitazone

This gentleman has non-alcoholic steatohepatitis (NASH) as evidenced by deranged liver function tests and fatty infiltration on ultrasound scan. NASH is commonly seen in type 2 diabetes and is associated with an increased body mass index. It usually resembles alcoholic liver disease but the history of alcohol intake in such people is either absent or only modest. The diagnosis of this condition is based on the exclusion of common liver disorders like viral hepatitis, alcoholic liver disease, drug induced and autoimmune liver disease (e.g. primary biliary cirrhosis). The gold standard confirmatory test for diagnosis is liver biopsy although this is rarely done as can be supported with non-invasive tests. NASH is associated with insulin resistance and diabetes. Pioglitazone has shown beneficial effects in improving NASH and improvement in insulin resistance. Weight gain is an adverse effect associated with pioglitazone. The patients should be encouraged to bring life style modification changes including regular exercise and weight loss. Reference: http://www.nejm.org/doi/pdf/10.1056/NEJMoa0907929

Question 42

A 35 week pregnant woman with a 10 year history of type 1 diabetes presents to A and E with features of nausea, vomiting and generally being unwell for the last 48 hours. She has recently received a course of steroids for foetal lung maturation. Her biochemistry results are as shown below:

		Normal Ranges
Blood sugar	14 mmol/L	(3.5-5.5)
Urine	sugar ++, ketones 3+	
pH	7.1	(7.35-7.45)
Bicarbonate	10 mmol/L	(22-26)
Chloride	95 mmol/L	(98-108)
PCO2	24 mmHg	(35-45)
PO2	104 mmHg	(80-100)
Sodium	144 mmol/L	(134-144)
Potassium	4.5 mmol/L	(3.5-5.5)
Lactic acid	3.5 mmol/L	(0.5-2.2)
Amylase	44 U/L	

Which is the likely underlying diagnosis?

- **A)** Acute adrenal insufficiency
- **B)** Acute pancreatitis
- **C)** Diabetic ketoacidosis (DKA)
- **D)** Lactic acidosis
- **E)** Methanol ingestion

Answer

Correct answer : Diabetic ketoacidosis (DKA)

This lady has recently received a course of steroids for foetal lung maturation, adversely affecting her glycaemic control. She has metabolic acidosis with a pH of 7.1 and serum bicarbonate levels of 10 mmol/L. Her blood sugars are mildly elevated and urinary ketone bodies are present. Essentially the diagnosis is diabetic ketoacidosis and a relatively mild increase in her blood sugar values is secondary to reduced carbohydrate intake due to nausea and vomiting. She should be treated with oral carbohydrates and her need for intravenous fluids and insulin should be closely monitored.

The criteria for DKA is:

- Plasma glucose: (>)11 mmol/L in DKA
- Arterial pH: 7.25-7.3 in mild DKA; 7.00-7.24 in moderate DKA ; less than 7.00 in severe DKA
- Serum bicarbonate: 15 to 18 mmol/L in mild DKA; 10 to 15 mmol/L in moderate DKA; less than 10 mmol/L in severe
- Urine and serum ketones: + in DKA
- Effective serum osmolality: variable in DKA
- Anion gap: more than 10 mmol/L in mild DKA; more than 12 mmol/L in moderate and severe DKA
- Mental status: alert in mild DKA; alert/drowsy in moderate DKA; stupor/coma in severe DKA.

According to NICE guidelines on diabetes in pregnancy (NICE clinical guidelines 63), patients with suspected DKA during pregnancy should be admitted immediately for level 2 critical care and provided with both medical and obstetric care.

Her anion gap is 39 mEq/L [Anion gap Na - (Cl + HCO3)]. Normal values for anion gap are 8-12 mEq/L. Causes of high anion gap acidosis include:

- Methanol
- Uraemia
- Diabetic ketoacidosis
- Paraldehyde
- Infection
- Lactic acidosis
- Ethylene glycol
- Salicylate

Question 43

A 64-year-old man was reviewed in clinic on a routine follow-up visit. He was known to have Type 2 DM for over 10 years and was currently on metformin 1g bd. He had suffered from an acute myocardial infarction about 3 years ago, which required rescue angioplasty for the left anterior descending artery. He was on atorvastatin, bisoprolol, clopidogrel and ramipril.

On examination, his body mass index was 31.2 Kg/m^2. He had pitting oedema, raised JVP and bilateral basal crepts on auscultation of chest.

Investigations:

HbA1c	77 mmol/mol (9.2%)
eGFR	65 mls/min/1.73m^2.

Which of the following is the most appropriate next step in his management based on current evidence?

- **A)** Glimepiride
- **B)** Empagliflozin
- **C)** Pioglitazone
- **D)** Repaglinide
- **E)** Saxagliptin

Answer

Correct answer : Empagliflozin

Explanation:

This 64-year-old man has sub-optimal glycaemic control apart from established cardiovascular disease (previous myocardial infarction) and clinical features of heart failure.

EMPA-REG trial is a double blind randomised placebo controlled trial which was first present at EASD (September 2015). Patients with Type 2 DM with established CVD or at high risk of CVD were randomised to receive empagliflozin (10 mg or 25 mg once a day) or a placebo.

The primary outcome of the study was composite of death from cardiovascular causes, non-fatal MI or non-fatal stroke.

Empagliflozin therapy was associated with a significantly lower risk of death from cardiovascular causes apart from significantly lower risk of death from any cause and hospitalisation for heart failure as compared to the placebo group.

Based on current evidence base, our high risk CVD patient will benefit from the addition of empagliflozin therapy as a second line agent. His renal function is normal and there is no obvious contraindication for use of this medication.

Reference:

- Boussageon R et al. Effect of intensive glucose lowering treatment on all cause mortality, cardiovascular death, and microvascular events in type 2 diabetes: meta-analysis of randomised controlled trials. BMJ 2011; 343.
- Zinman B et al. Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes.
- N Engl J Med 2015; 373:2117-2128.

Question 44

A 58-year-old lady is brought to the accident and emergency department by her daughter. She states that her mother was experiencing palpitations, sweating and having difficulty speaking. The patient appears to be confused, disoriented but conscious and is able to swallow. Her medical history is significant for type 2 diabetes and she is currently taking glimepiride 2 mg OD. According to her daughter, the patient has experienced similar episodes over the last two months. An ECG was performed which was normal. Her random plasma glucose level was 2.9 mmol/L. What would be the most appropriate treatment?

- **A)** 1 mg of glucagon IM
- **B)** 2 tubes of 40% glucose gel, directly in the mouth
- **C)** 75 ml of 20% glucose IV over 15 mins
- **D)** 150 ml of pure fruit juice
- **E)** Start 10% glucose at 100ml/hr IV

Answer

Correct answer : 2 tubes of 40% glucose gel, directly in the mouth

Explanation:

It is important to recognise symptoms of hypoglycaemia which can be mild, moderate or severe. This patient is a known diabetic, is taking sulfonylureas and has presented with autonomic (palpitations, sweating) and neuroglycopenic (confusion, disorientation and difficulty in speaking) symptoms of hypoglycaemia. Her random plasma glucose level was found to be 2.9mmol/L and it is likely due to sulfonylureas. The risk of hypoglycaemia with sulfonylureas is frequently prolonged, comparable to insulin and more common in elderly patients and those with renal impairment.

Hypoglycaemia should be treated as an emergency regardless of the level of consciousness. Treatment depends on whether the patient is having mild, moderate or severe symptoms. This patient has moderate symptoms and appears to be confused and disoriented but is able to swallow. According to JBDS guidelines, such patients should be initially given 1.5-2 tubes of 40% glucose gel that is squeezed into the mouth between teeth and gums or give glucagon 1mg IM. Glucagon should not be given in this case as it may be ineffective in repeated hypoglycaemia and oral hypoglycaemic agent-induced hypoglycaemia. IV glucose should be given if the patient is having severe hypoglycaemia while oral quick-acting carbohydrates are given in mild symptoms.

Reference:

- JBDS-IP (Revised January 2020).The Hospital Management of Hypoglycaemia in Adults with Diabetes Mellitus

Question 1

A 45 year old lady recently diagnosed with type 2 diabetes is managed by diet and exercise alone and has an HbA1c of 47.5 mmol/mol (6.5%) (<42.1 mmol/mol (6)). Her BMI is 32 kg / m^2 and her blood pressure is 144 / 74 mmHg.

She has a 13 year old daughter and is concerned about the potential risk of her daughter subsequently developing type 2 diabetes.

Which of the following is the correct lifetime risk of type 2 diabetes for this lady's daughter?

- **A)** 1 in 2
- **B)** 1 in 3
- **C)** 1 in 10
- **D)** 1 in 20
- **E)** 1 in 40

Answer

Correct answer : 1 in 10

The incident diabetes risk in siblings and offspring of patients with type 2 diabetes is approximately 10%. The background population risk for type 2 diabetes is around 2-5%, while the risk of incident type 2 diabetes in a monozygotic twin of a patient with type 2 diabetes is around 1 in 3.

Question 2

A 33 year old lady with a 10 year history of type 1 diabetes has been converted from twice daily Novomix to a basal bolus insulin regimen comprising of insulin glargine and novorapid three months previously at a total daily dose of 72 units. On review in the clinic her glycaemic control has improved since her insulin regimen change with her current Hba1c measuring 65.0 mmol/mol (8.1 %) (<42.1 mmol/mol (6)) compared with 73.8 mmol/mol (8.9%) (<42.1 mmol/mol (6)) prior to her regimen change. She is however unclear as to how to modify her prandial insulin doses according to her diet.

Which of the following is the most appropriate initial advice for this lady with respect to adjusting her prandial insulin dose?

- **A)** 0.5 units of insulin per 10 gram of dietary carbohydrate
- **B)** 1 units of insulin per 10 gram of dietary carbohydrate
- **C)** 2 units of insulin per 10 grams of dietary carbohydrate
- **D)** 3 units of insulin per 10 grams of dietary carbohydrate
- **E)** 4 units of insulin per 10 grams of dietary carbohydrate

Answer

Correct answer : 1 units of insulin per 10 gram of dietary carbohydrate

The DAFNE patient education program suggests that patients should initially adjust prandial insulin doses by 1 unit according to each 10 gram of dietary carbohydrate. This initial ratio may subsequently be modified according to response and the influence of other factors such as exercise.

Question 3

A 21 year old man has a 4 year history of type 1 diabetes with good glycaemic control exemplified by a most recent HbA1c measurement of 47.5 mmol/mol (6.5%) (<42.1 mmol/mol (6)). His current medication includes once daily insulin glargine at a dose of 8 units combined with preprandial humalog at a dose of 4 units prior to each meal. He experiences occasional hypoglycaemic episodes and questions his diagnosis. Reviewing his notes he was found to have presented with ketoacidosis but cytoplasmic islet cell antibody serology was negative. What percentage of patients with type 1 diabetes will exhibit high titres of cytoplasmic islet cell antibodies?

- **A)** 5 - 10%
- **B)** 20 - 25%
- **C)** 30 - 40%
- **D)** 60 - 80%
- **E)** 100%

Answer

Correct answer : 60 - 80%

Cytoplasmic islet cell antibodies (ICA) are IgG antibodies which can react on frozen sections of human, rat or mouse pancreas. High titres of ICA are found in up to 80% of newly diagnosed patients with type 1 diabetes, in approximately 3% of first degree relatives and in 0.2% of the general population. The great majority of patients developing type 1 diabetes express autoantibodies reacting to more than one antigen. Relatives expressing a single autoantibody (e.g. Anti-GAD, with restricted ICA) show a lower rate and slower progression to overt diabetes.

Question 4

A 41 year old lady is referred to the diabetes clinic following presentation to her primary care physician with a 5 month history of lethargy and increasing thirst but denies any weight loss. On examination, her blood pressure is 125/70 mmHg, her BMI is 25 kg /m^2 and her waist circumference is 73.4 cm.
Investigations reveal:

		Normal Ranges
Fasting plasma glucose	12.9 mmol/l	(3.5 - 5.6)
Random plasma glucose	14.7 mmol/l	(3.5 - 5.6)
Cholesterol	4.8 mmol/l	(<5)
Triglyceride	1.7 mmol/l	(0.9 - 2.2)
HDL-C	1.4 mmol/l	(0.9 - 1.9)
LDL-C	2.9 mmol/l	(<2)
TSH	0.7 mu/l	(0.32 - 5)
GAD Antibodies	Positive	

Which of the following is the correct diagnosis for this lady?

- **A)** Impaired glucose tolerance
- **B)** Latent Autoimmune Diabetes in Adults (LADA)
- **C)** Metabolic Syndrome
- **D)** Type 1 diabetes
- **E)** Type 2 diabetes

Answer

Correct answer : Latent Autoimmune Diabetes in Adults (LADA)

Positive glutamic acid decarboxylase antibody (GAD) serology suggests the diagnosis to be LADA - latent autoimmune diabetes in adults. This lady has no features of the metabolic syndrome or type 2 diabetes and is unlikely to have type 1 diabetes as she reports no weight loss which is a cardinal feature of absolute insulin deficiency. LADA is a form of type 1 diabetes with slow progression to insulin dependency and can be distinguished from people with type 2 diabetes by the presence of GAD autoantibodies. There is no consensus on the optimum treatment of LADA, however a recent Cochrane review concluded that a sulphonylurea should not be the first line treatment since it may be associated with a more rapid progression to insulin dependence.

Question 5

A 35 year old school teacher is referred to clinic for assessment of and management of his diabetes. He was diagnosed with diabetes 3 years previously on the basis of elevated fasting blood glucose levels and has subsequently experienced good glycaemic control on oral hypoglycaemic therapy. He denies any weight loss, has never experienced ketosis and has an elder sister who was diagnosed with diabetes 12 years previously at the age of 24. On examination his blood pressure is 135/75 mmHg, his body weight is 75 kg and his BMI is 25.5 kg / m^2. His current medication includes metformin 1 gram twice daily and gliclazide 80 mg twice daily.
Investigations reveal:

		Normal Ranges
HbAlc	58.5 mmol/mol (7.5%)	(<42.1 mmol/mol (6))
Fasting Plasma Glucose	6.9 mmol/l	(<6)
Total cholesterol	4.5 mmol/l	(<4)
TSH	0.1 mu/l	(032 - 5.5)
TSH receptor antibodies	Negative	
eGFR	96 ml/min/1.73 m^2	(90 - 110)
GAD antibodies	Negative	

Which of the following is the most likely correct diagnosis for this young man?

- **A)** Latent Autoimmune Diabetes in Adults (LADA)
- **B)** Maturity onset diabetes of the young (MODY)
- **C)** Schmidt syndrome
- **D)** Type 1 diabetes
- **E)** Type 2 diabetes

Answer

Correct answer : Maturity onset diabetes of the young (MODY)

The most likely diagnosis for this patient is MODY, suggested by the presence of a first degree relative presenting with diabetes < 25 years coupled with the fact that this patient has no evidence of ketosis and has corrected fasting blood glucose for at least 2 years without insulin. The diagnosis of MODY in this case is also supported by the absence of features of the metabolic syndrome, obesity and negative GAD serology.

Question 6

A 33 year primary school teacher is referred to clinic by her GP. She has recently moved into the area having been diagnosed with diabetes 5 years previously and commenced immediately on insulin. She however denies any history of weight loss or osmotic symptoms prior to initiation of insulin. She has a younger brother recently diagnosed with diabetes. Her glycaemic control has always been good and she describes hypoglycaemic symptoms once to twice weekly. On examination her BMI is 25 kg / m^2 her body weight is 64 kg, her waist circumference is 69 cm, her blood pressure is 120 / 65 mmHg and her visual acuity is 6 / 6 in both eyes. Her current medication includes insulin glargine 8 units at night combined with novorapid 4 units prior to lunch and dinner.
Investigations reveal:

		Normal Ranges
Hba1c	45.4 mmol/mol (6.3%)	(<42.1 mmol/mol (6))
Islet cell antibodies	Negative	
GAD antibodies	Negative	
TSH	0.36 mu/l	(0.32 - 5)
eGFR	>99 ml/min 1.73m2	(90 - 110)

What is the genetic basis of this lady's diabetes?

- **A)** Autosomal co-dominant
- **B)** Autosomal dominant
- **C)** Autosomal recessive
- **D)** Polygenic
- **E)** X-linked recessive

Answer

Correct answer : Autosomal dominant

This patient has Maturity onset diabetes of the young (MODY) based on the clinical presentation. The diagnosis of MODY is supported the following clinical characteristics

- Mild to moderate hyperglycaemia (typically 130-250 mg/dl, or 7-14 mM) discovered before 30 years of age.
- A first degree relative with a similar degree of diabetes.
- Absence of positive antibodies or other autoimmune conditions (e.g thyroiditis) in patient and family.
- Persistence of a low insulin requirement (e.g. less than 0.5 u/kg/day) past the usual "honeymoon" period.
- Absence of obesity (though obese people can get MODY), or other problems associated with type 2 diabetes or
- Cystic kidney disease in patient or close relatives.
- Non-transient neonatal, or apparent type 1 diabetes with onset before 6 months of age.

Inheritance is autosomal dominant with penetrance of 40 – 90%, thus most patients will have other family members with diabetes.

Question 7

A 51 year old man with recently identified type 2 diabetes currently managed with lifestyle modification alone undergoes a mixed meal tolerance test with measurement of glucose, insulin and glucagon profiles over a 4 hour period.

Which of the following glucose, insulin and glucagon profiles would you expect to occur in this gentleman compared to an age matched healthy volunteer following a mixed meal tolerance test?

- **A)** Increased plasma glucose, reduced early phase insulin secretion, reduced glucagon secretion
- **B)** Increased plasma glucose, reduced early phase insulin secretion, elevated glucagon secretion
- **C)** Increased plasma glucose, exaggerated early phase insulin secretion, reduced glucagon secretion
- **D)** Increased plasma glucose, delayed early phase insulin secretion, no difference in glucagon secretion
- **E)** Increased plasma glucose, no difference in insulin secretion, elevated glucagon secretion.

Answer

Correct answer : Increased plasma glucose, reduced early phase insulin secretion, elevated glucagon secretion

Beta and alpha cell dysfunction are characteristic features of the pathophysiology of type 2 diabetes. Beta cell function is reduced by up to 70% according to data from UKPDS at the point of type 2 diabetes diagnosis. The earliest manifestation of beta cell dysfunction occurs in the form of reduced and delayed postprandial early phase insulin secretion. Alpha cell dysfunction is manifest as elevated plasma glucagon levels compared to healthy subjects which remain inappropriately elevated following meal ingestion.

Question 8

A 45 year old man with a 6 month history of diet controlled type 2 diabetes undergoes a 2,500 kcal 4 hour mixed meal tolerance test as part of a research program. Peak insulin concentrations are measured after 2 hours with a level of 48 pmol/l being achieved with a peak glucose concentration of 14. 8 mmol/l being achieved after 90 minutes
Which of the following is a feature of pancreatic beta cell function?

- **A)** Beta cells account for 30% of the Endocrine cell mass.
- **B)** C-Peptide is secreted with insulin in a 2:1 molar ratio
- **C)** C-peptide is a byproduct of insulin proteolysis
- **D)** Early phase insulin secretion is delayed and diminished in people with impaired glucose tolerance
- **E)** Insulin is produced by proteolytic cleavage from pro-insulin

Answer

Correct answer : Insulin is produced by proteolytic cleavage from pro-insulin

Insulin is produced in the pancreatic beta cell by proteolytic cleavage from pro-insulin resulting in a by-product, namely c-peptide which is secreted together with insulin in a 1:1 molar ratio. Beta cells account for between 70 – 80% of the endocrine cell mass of the pancreas and contain chromogranin A which is an acidic 48kDa protein which has a putative function as a prohormone. Delayed, but exaggerated early phase insulin secretion is a feature of early glucose intolerance, as glucose intolerance progresses to type 2 diabetes, with associated progressive beta cell dysfunction, early phase postprandial insulin secretion becomes both delayed and blunted.

Question 9

A 59 year old lady with a 4 year history of type 2 diabetes is reviewed in clinic. On examination her BMI is 33 kg / m^2 and her blood pressure is 145 / 65 mmHg. She is generally well but is concerned about the possibility of cardiovascular disease since her father suffered with a myocardial infarction at the age of 61 years and she has recently read an article outlining the link between diabetes and cardiovascular disease.
Investigations reveal:

		Normal Ranges
total Cholesterol	4.8 mmol/l	(<5)
LDL-Cholesterol	2.8 mmol/l	(< 3)
HDL-Cholesterol	1.1 mmol/l	(0.9 - 1.9)
Hba1c	54.1 mmol/mol (7.1%)	(<42.1 mmol/mol (6))
Plasma Triglyceride	1.9 mmol/l	(0.9 - 2.2)
TSH	1.9 mu/l	(0.32 - 5)

Which of the following parameters is the most important coronary heart disease risk factor in this lady?

- **A)** Hba1c
- **B)** HDL-Cholesterol
- **C)** LDL-Cholesterol
- **D)** Total cholesterol
- **E)** Systolic Blood pressure

Answer

Correct answer : LDL-Cholesterol

The UKPDS cardiovascular risk assessment model for patients with type 2 diabetes identified LDL-C as the most important individual determinant of coronary heart disease, followed in sequential order by HDL-C, Hba1c, systolic blood pressure and smoking.

Question 10

A 28 year old man is referred by his GP following presentation with polydipsia, weight loss and general malaise. He has no previous medical history of note and no family history of note. On examination his BMI is 27 kg / m^2 and his blood pressure is 133 / 73 mmHg.
Investigations reveal

		Normal Ranges
Fasting plasma glucose	15.9 mmol/l	(<5.6)
Hba1c	86.9 mmol/mol (10.1%)	(<42.1 mmol/mol (6))

Which of the following is a feature of the pathophysiology of type 1 diabetes?

- **A)** Has a single susceptibility locus
- **B)** HLA genes on chromosome 6 are closely linked to autoimmune process
- **C)** Malnutrition in utero is a risk factor
- **D)** Mechanism of autoimmunity is B-cell mediated
- **E)** Obesity is a major risk factor

Answer

Correct answer : HLA genes on chromosome 6 are closely linked to autoimmune process

Multiple HLA loci on chromosome 6 are linked with the pathophysiology of type 1 diabetes. Obesity is not a contributory factor to the pathophysiology of type 1 diabetes, however there is an increasing incidence of obesity in patients with type 1 diabetes which contributes to challenges in the clinical management of such patients. Immune mediated islet cell destruction in type 1 diabetes is primarily CD4 +T-cell mediated, with class II HLA molecules being critical to the presentation of antigens to CD4+ T cells. It has been postulated that the predisposing DR3 / DR4 alleles for type 1 diabetes arises as a result of the more efficient presentation and binding of a specific ‘diabetogenic’ peptide. Intrauterine malnutrition is a recognised risk factor in the aetiology of type 2 diabetes – the so called Barker hypothesis.

Question 11

A 44 year old lady has recently been diagnosed with type 2 diabetes. She is currently receiving no medication and has an HbA1c of 51.9 mmol/mol (6.9%. Her GP suggests that her identical twin sister should be screened for diabetes as well.

What is the lifetime risk of this lady's twin sister having type 2 diabetes or any abnormality of glucose metabolism?

- **A)** < 5%
- **B)** 5 - 10%
- **C)** 10 - 20%
- **D)** 30 - 50%
- **E)** > 70%

Answer

Correct answer : > 70%

Using clinical diabetes as the criterion, most twin studies have demonstrated a concordance rate for monozygotic twins of between 45 – 95% and for dizygotic twins between 3 and 37%. When glucose tolerance tests are performed in ‘non-diabetic’ monozygotic co-twins available data suggests that the concordance rate is usually over 70%.

Concordance rate for type II diabetes mellitus in monozygotic twins: actuarial analysis.

Question 12

A 55 year old man undergoes a 75 gram oral glucose tolerance subsequent to a fasting plasma glucose measurement of 8.3 mmol/l (< 6) conducted by his GP. The results of his 75 gram oral glucose tolerance test reveal a fasting plasma glucose of 7.1 mmol/l (<5.6) and a 2 hour post-challenge plasma glucose of 12.2 mmol/l (< 7.8)

Which of the following is a recognised feature of type 2 diabetes?

- **A)** 30% of patients presenting with acute coronary syndrome will have undiagnosed type 2 diabetes
- **B)** C-Peptide is usually low or absent at diagnosis
- **C)** Genetic mutation has been identified in up to 30% of patients at diagnosis
- **D)** Has a low identical twin concordance
- **E)** Insulin levels are elevated comparable to the degree of glycaemia at diagnosis

Answer

Correct answer : 30% of patients presenting with acute coronary syndrome will have undiagnosed type 2 diabetes

Up to 1/ 3 of patients presenting with acute coronary syndromes, including myocardial infarction will on screening, despite having no previous history of glucose intolerance, have type 2 diabetes. A similar proportion of patients presenting with acute cerebrovascular syndromes (stroke / TIA) will also have previously unidentified type 2 diabetes. C-peptide levels are usually present or may even be elevated at diagnosis in patients with type 2 diabetes as consequence of hyperinsulinemia related to insulin resistance. This hyperisnulinemia is not appropriate to the level of glycaemia. Identical twin concordance is high (45 – 95%) in twin studies of patients with type 2 diabetes.

Question 13

A 49 year old man attends clinic for review. He has a 2 year history of type 2 diabetes which was diagnosed following admission to hospital with a troponin positive cardiac event. His current medication includes simvastatin 40 mg at night, metformin 500 mg three times daily, aspirin 75 mg once daily, Perindopril 4 mg once daily and Bisoprolol 2.5 mg once daily.

On examination, his BMI is 30 kg /m^2, his blood pressure is 141/79 mmHg and his pulse is 62 beats per minute.

Investigations reveal:

		Normal Ranges
Hba1c	51.9 mmol/mol 6.9%	(<42.1 mmol/mol (6))
Total Cholesterol	3.9 mmol/l	(<5)
LDL-C	1.8 mmol/l	(<2)
HDL-C	0.8 mmol/l	(0.9 - 1.8)
Fasting Plasma TG	2.7 mmol/l	(0.9 - 2.2)
TSH	4.3 mu/l	(0.32 - 5)

Which of the following would be the most appropriate treatment option to optimise this patient's lipid profile?

- **A)** Switch Simvastatin to Atorvastatin
- **B)** Add Ezetimibe
- **C)** Add Fenofibrate
- **D)** Add Omega-3 fish oil
- **E)** Switch Simvastatin to Ezetimibe

Answer

Correct answer : Switch Simvastatin to Atorvastatin

In this scenario, switching to high intensity statin; atorvastatin is the best option. It is recommended to use up to maximum of 80 mg dose before considering adding ezetimibe. There is no role for fibrates, niacin or omega 3 fatty acids.

https://www.nice.org.uk/advice/ktt3/chapter/evidence-context#bile-acid-sequestrants-fibrates-and-nicotinic-acid

Question 14

A 53 year old lady with a 3 year history of type 2 diabetes is reviewed in clinic; she has a previous history of hypothyroidism but has no other medical history of note. Her current medication includes metformin 500 mg three times a day, simvastatin 20 mg at night, ramipril 2.5 mg once a day and thyroxine 100 mcg once a day.

On examination her BMI is 32 kg /m^2 blood pressure 135/85 mmHg and her pulse is 62 beats per minute.

Investigations reveal:

		Normal Ranges
Hba1c	58.5 mmol/mol 7.5%	(<42.1 mmol/mol (6))
total cholesterol	6.3 mmol/l	(<5)
LDL-C	4.1 mmol/l	(<2)
triglyceride	2.1 mmol/l	(0.9 - 2.2)
eGFR	> 96 /min / 1.73 m^2	(90 - 110)
TSH	8.6 mu / l	(0.32 - 5.5)
Free T4	10.9 pmol/l	(9.3 - 23.4)

Which of the following is the most appropriate treatment option to optimise this lady's lipid profile?

- **A)** Add Fenofibrate
- **B)** Commence Atorvastatin
- **C)** Increase Simvastatin
- **D)** Increase Metformin
- **E)** Increase thyroxine

Answer

Correct answer : Increase thyroxine

This lady appears to have sub-optimal thyroid hormone replacement which is likely to contribute to her dyslipidaemia. Hypothyroidism is a recognised risk factor for lipid lowering therapy associated myotoxicity, therefore prior to escalating her specific lipid lowering medications it is important to correct her thyroid profile.

Question 15

A 65 year old lady is referred to the clinic for insulin initiation. She has previously tried GLP-1 RA and failed to respond. She has a 7-year history of type 2 diabetes with deteriorating glycaemic control over the last 2 years resulting in a most recent HbA1c measuring 76.0 mmol/mol (9.1%). Her current medication includes metformin 1g BD, gliclazide 160 mg BD, ramipril 5 mg OD, furosemide 40 mg OD, simvastatin 40 mg od and bisoprolol 1.25 mg OD. She has a previous history of ischaemic heart disease having been admitted to hospital 8 months previously with an episode of heart failure.

On examination, her BMI measures 35 kg/m^2, her blood pressure 140/80 mmHg and she has evidence of background retinopathy on retinal screening. She has been previously intolerant of exenatide due to nausea and had no significant response when commenced on sitagliptin. You contemplate insulin initiation for her but she informs you that she is worried about commencing insulin as she lives alone and is worried about hypoglycaemia when commenced on insulin. Which of the following insulin regimens would be the most appropriate for this lady in terms of hypoglycaemia avoidance?

- **A)** Once daily insulin long acting analogue
- **B)** Once daily NPH insulin
- **C)** Thrice daily preprandial novorapid
- **D)** Twice daily biphasic insulin aspart
- **E)** Twice daily NPH insulin

Answer

Correct answer : Once daily insulin long acting analogue

This lady's primary concern with respect to insulin therapy is minimising hypoglycaemia risk. Her BMI is also elevated thus a secondary consideration would relate to the minimization of any weight gain associated with exogenous insulin therapy. Basal insulin analogues such as insulin detemir and glargine are associated with reduced hypoglycaemia risk compared with NPH insulin, while results of the 4T study demonstrated that insulin initiation with detemir in patients receiving on-going metformin and sulphonylurea combination therapy was associated with reduced hypoglycaemia and less weight gain compared with either TDS preprandial novorapid or twice daily novomix 30 regimens.

Question 16

A 42 year old South Asian gentleman is referred to the diabetic clinic by his GP. He has a 5 year history of type 2 diabetes. He complains of feeling tired and has a previous history of ischaemic heart disease.

On examination BMI 34 kg m^2, pulse 52 bpm, blood pressure 148/78 mmHg. Current medication consists of 'Novomix 30/70' mixed insulin - 42 IU twice daily, metformin 500 mg twice daily, simvastatin 20 mg od, aspirin 75 mg od, enalapril 20 mg od, atenolol 50 mg od.
Investigations

		Normal Ranges
Hbalc	62.8 mmol/mol (7.9%)	(42.1 mmol/mol <(6))
Total Cholesterol	6.9 mmol/l	(<5)
LDL-Cholesterol	4.5 mol/l	(< 3)
Triglyceride	2.9 mmol/l	(0.9 - 2.2)
U + Es	Normal	
TSH	32.8 mu / l	(0.3 - 5.5)
Free T4	6.9 pmol / l	(9.8 - 23.6)

Which of the following is the most appropriate approach to optimise this patient's lipid profile?

- **A)** Improve glycaemic control
- **B)** Commence thyroxine
- **C)** Commence fenofibrate
- **D)** Commence omega 3 fish oil
- **E)** Increase simvastatin dose

Answer

Correct answer : Commence thyroxine

This patient is hypothyroidic and correction of his thyroid status will also improve both his glucose control and lipid profile. Increasing the statin dose or commencing a fibrate is not appropriate as hypothyroidism is a risk factor for dyslipidaemia per se and is also associated with increased risk of myotoxicity with lipid-lowering therapies. Omega-3 fish oils are not routinely recommended for use in this setting.

Question 17

A 35 year old lecturer with a 14 year history of type 1 diabetes attends clinic for review. He describes an erratic blood glucose profile on self blood glucose monitoring with unpredictable episodes of hypoglycaemia occurring at a frequency of up to 3 to 4 episodes per week despite optimal education which has resulted in recent loss of hypo awareness.
On examination blood pressure 125 / 75 mmHg, fundoscopy reveals background retinopathy in the left eye and examination of injection sites reveals no evidence of lipohypertrophy. Current medication includes basal insulin glargine combined with preprandial insulin aspart (novorapid) with dose adjustment of both insulins according to self monitored blood glucose levels and dietary carbohydrate content.

		Normal Ranges
		Normal Ranges
Hbalc	65 mmol/mol (8.1%)	(42.1 mmol/mol (<6))
Total Cholesterol	3.9 mmol/l	(<5)
Plasma Triglyceride	1.2 mmol/l	(0.9 - 2.2)
eGFR	98 ml/ min / 1.73 m 2	(90 - 110)
TSH	0.4 mu / l	(0.32 - 5.5)
albumin/creatinine ration	0.4 mg / mmol	(<2.5)

Which of the following is the most appropriate approach for the management of this patient's blood glucose control?

- **A)** Convert to a three times daily Mix 50 regimen
- **B)** Add metformin
- **C)** Continuous subcutaneous insulin infusion (insulin pump)
- **D)** Convert basal insulin glargine to insulin detemir
- **E)** Convert once daily basal insulin glargine to twice daily insulin glargine

Answer

Correct answer : Continuous subcutaneous insulin infusion (insulin pump)

This patient fulfils current NICE guideline criteria for CSII therapy, in that he is failing to achieve optimal blood glucose control despite appropriate education and insulin therapy in the setting of variable blood glucose profiles and frequent hypoglycaemic episodes.

Question 18

A 51 year old gentleman is referred by his GP for review of his glucose control and insulin dosage. He has a 7 year history of type 2 diabetes. He has a previous history of ischaemic heart disease having been commenced on insulin following his myocardial infarction 3 years previously.

On examination, body weight is 144 kg, BMI 51 Kg / m^2 pulse 67 bpm, blood pressure 160/88 mmHg. He has already tried an exercise regime and other weight loss measures recommended by his doctor with little effect. His current mediation includes metformin 1 gram twice daily, simvastatin 40 mg daily, novomix 30/70 mixed insulin 114 units in the morning, 120 units evening time, ramipril 10 mg daily, bisoprolol 5 mg daily and aspirin 75 mg daily having been previously intolerant of orlistat.

Investigations reveal

		Normal Ranges
Hba1c	83.6 mmol/mol (9.8%)	(42.1 mmol/mol (<6))
Total Cholesterol	4.1 mmol/l	(<5)
Plasma triglyceride	2.5 mmol/l	(0.9 - 2.2)
TSH	2.9 mu l	(0.32 - 5.5)
eGFR	58 ml / min / 1.73 m^2	(90 - 110)
albumin creatinine Ratio	5.5 mg / mmol	(<2.5)

Which of the following is the most appropriate therapy option for this patient?

- **A)** Conversion to insulin detemir
- **B)** Conversion from insulin to exenatide
- **C)** Addition of exenatide
- **D)** Addition of orlistat
- **E)** Referral for bariatric surgery.

Answer

Correct answer : Referral for bariatric surgery.

This patient fulfils referral criteria for bariatric surgery in that he is morbidly obese (BMI above 40) with associated co-morbidities including poorly controlled diabetes, hypertension and ischaemic heart disease. Conversion to another insulin regimen is unlikely to have additional benefits. Long-term weight loss response to gastroplasty or banding is between 16 and 25% at 10 years. Bariatric surgery has been shown to result in a 39% relative risk reduction in all-cause mortality at 10 years post surgery, while diabetes remission rate at 10 years is around 40%.

Question 19

A 70 year old lady is referred to clinic for specialist assessment. She has a 7 year history of type 2 diabetes and has a background history of ischaemic heart disease having suffered a myocardial infarction 2 years previously and had an echocardiogram at this point revealing an impaired left ventricular ejection fraction of 40%. Her current treatment includes metformin 1 gram bd, gliclazide 160 mg bd, simvastatin 40 mg od, aspirin 75 mg od, lisinopril 20 mg od, furosemide 40 mg od, bisoprolol 5 mg od.

Clinical examination reveals BMI 33 kg /m^2, blood pressure 143/67 mmHg, pulse 65 bpm, her chest is clear to auscultation and there is no evidence of heart failure.
Investigations reveal:

		Normal Ranges
		Normal Ranges
Hba1c	76 mmol/mol	(9.1%)
Cholesterol	4.4 mmol/l	(< 5)
LDL-C	2.4 mmol/l	(< 3)
Triglyceride	2.2 mmol/l	(0.9 - 2.2)
eGFR	65 ml / min/ 1.73 m2	(90 - 110)
TSH	2.5 mu / l	(0.3 - 5.5)

Which of the following is the most appropriate treatment option for reducing this patient's blood glucose?

- **A)** Empagliflozin
- **B)** Exenatide
- **C)** Insulin glargine
- **D)** Pioglitazone
- **E)** Vildagliptin

Answer

Correct answer : Empagliflozin

Based on the data from the EMPA-REG outcome trial, there wasa 37% reduction in cardiovascular mortality associated with empagliflozin versus placebo. On this basis it woul seem the most logical choice of treatment in this patient scenario. The patient's egfr also needs to be above 60 ml/min to enable the introduction of a SGLT-2 inhibitor. In this scenrio also, Liraglutide would also be an appropriate choice as the LEADER trial demonstrated favourable CV outcome data. These agents would be more appropriate than insulin in this scenario as the patient would be expected to gain weight further.

Question 20

A 60 year old lady with a 6 month history of type 2 diabetes and past history of hypertension attends a community diabetes clinic for review. She is generally well and is currently receiving no oral hypoglycaemic therapy. On examination BP 150 / 78 mmHg, BMI 28 Kg / m^2 Body weight 63 kg, waist circumference 78 cm and no evidence of microvascular complications can be identified. Current medication includes lisinopril 20 mg OD, simvastatin 20 mg OD and aspirin 75 mg OD.
Investigations reveal:

		Normal Ranges
		Normal Ranges
Hba1c	56.3 mmol/mol (7.3%)	(42.1 mmol/mol (<6))
Total Cholesterol	4.8 mmol/l	(<5)
Plasma triglyceride	1.7 mmol/l	(<1.7)
eGFR	56 ml /min / 1.73 m2	(90- 110)
Fasting Plasma Glucose	6.1 mmol/l	(3.5 - 5.5)
Albumin/creatinine ratio	4.1 mg / mmol	(<3.5)
Serum creatinine	128 micromol/l	(50 - 110)
TSH	1.2 mu / l	(0.32 - 5.5)

Which of the following is the most appropriate oral hypoglycaemic agent for this lady?

- **A)** Dapagliflozin
- **B)** Gliclazide
- **C)** Metformin
- **D)** Pioglitazone
- **E)** Sitagliptin

Answer

Correct answer : Metformin

Most guidelines recommend metformin as first line therapy in type 2 diabetes provided eGFR is greater than 30 ml/min/1.73m^2. In this patient the eGFR is 56 and the modestly elevated creatinine is not a contraindication to treatment. Metformin in this patient would offer potential reductions in mortality according to published data and would be the first choice for treatment.
Reference:
NICE guidance as pdf

Question 21

You are contacted by a GP colleague regarding an elderly lady with a history of type 2 diabetes, hypertension, ischaemic heart disease and features of vascular dementia. She is receiving multiple medications and her GP is concerned about the risk of drug interactions particularly with respect to the risk of hypoglycaemia.

Which of the following drugs taken by this lady may result in an increased risk of hypoglycaemia in patients with diabetes?

- **A)** Isosorbide mononitrate
- **B)** Nifedipine
- **C)** Low dose aspirin
- **D)** Omeprazole
- **E)** Simvastatin

Answer

Correct answer : Low dose aspirin

Low dose aspirin has been associated with the development of hypoglycaemia related to a stimulatory effect of aspirin on the beta cell mediated via inhibition of prostaglandin synthesis. In larger doses salicylates can have detrimental effects on glucose homeostasis resulting from inhibition of oxidative phosphorylation with a consequent impairment in glucose oxidation. Other commonly used agents which may increase the risk of hypoglycaemia, particularly in the elderly include ACE-inhibitors via mechanisms involving improved insulin sensitivity. Statins may have a diabetogenic risk. Nitrates and PPIs have no effect on glucose homeostasis, while nifedipine may have detrimental effects on glucose homeostasis.

Question 22

A 69 year old lady with a 4 year history of type 2 diabetes attends the clinic for annual review. She is currently taking metformin 1 g bd together with lisinopril 20 mg daily. She is well and little is noted on examination other than a BMI of 28.2 kg/m^2 and a blood pressure of 144/84 mmHg. She has an HbA1c of 58 mmol/mol (7.5%)(42.1 mmol/mol (<6)).

Which of the following would be the most appropriate approach to the further management of her hyperglycaemia?

- **A)** Add exenatide
- **B)** Add gliclazide
- **C)** Add pioglitazone
- **D)** Add liraglutide
- **E)** Continue with metformin alone

Answer

Correct answer : Add gliclazide

NICE would recommend the addition of a sulphonylurea/DPP-IV/pioglitazone or SGLT-2 inhibitor to metformin in such a patient in whom HBA1c remains above or equal to 58 mmol/mol (7.5%). Consideration should be given to swapping the sulphonylurea for a DPP-IV/SGLT-2 inhibitor if the SU is contraindicated or if there is significant risk of hypoglycaemia. In this postmenopausal woman pioglitazone is relatively contra-indicated due to fracture risk. The mechanism of action of the sulphonylurea class of drugs results in glucose-independent insulin release. Consequently sulphonylurea therapy may be associated with both hypoglycaemia and weight gain. Glibenclamide has the longest half life (approximately 16 hours) of all sulphonylureas with breakdown into metabolically active metabolites so that glibenclamide is the agent associated with the highest risk of hypoglycaemia.

NICE Algorithm for treating T2DM

Question 23

A 51 year old man with a 12 month history of diet controlled type 2 diabetes has an Hba1c of 7.4% (42.1 mmol/mol(<6)). On examination his BMI is 33 kg/m^2 and his blood pressure is 134/88 mmHg. He is consequently commenced on metformin at a starting dose of 500 mg BD. Which of the following is a recognized feature of metformin therapy?

- **A)** Metformin improves hepatic glucagon sensitivity
- **B)** Metformin undergoes both hepatic and renal clearance
- **C)** Metformin decreases splanchnic glucose turnover
- **D)** Metformin reduces hepatic and peripheral fatty acid synthesis
- **E)** Metformin may undergo significant drug interactions with warfarin, cimetidine and ACE-inhibitors.

Answer

Correct answer : Metformin reduces hepatic and peripheral fatty acid synthesis

Metformin has a variety of metabolic effects, although its complete mechanism of action is yet to be fully understood. Metformin improves insulin sensitivity, with recent data suggesting an increase in AMP kinase activity mediating an increase in glucose utilization and fatty acid oxidation both in the liver and peripheral tissues. The primary site of action of metformin appears to be the liver with suppression of hepatic glycogenolysis, gluconeogenesis and an increase in splanchnic glucose turnover all being involved in the glucose lowering effects of metformin. It is excreted almost unchanged in the urine, more by tubular secretion than by glomerular filtration; hence metformin is contraindicated in significant renal impairment due to an increased risk of metabolic acidosis, particularly in the presence of an inter-current illness or in the context of other conditions associated with tissue hypoxia. Consequently conditions associated with an increased risk of tissue hypoxia such as severe heart failure and respiratory diseases represent contraindications to metformin. Metformin may reduce intestinal vitamin B12 absorption and only undergoes drug interactions with cimetidine.

Question 24

A 49 year old man with a 12 month history of diet controlled type 2 diabetes has an Hba1c of 51.9 mmol/mol (6.9%)(42.1 mmol/mol(<6)), a BMI of 31 kg /m^2 and blood pressure of 165/89 mmHg. He is consequently commenced on ramipril at a starting dose of 2.5 mg once daily. Which of the following is a recognised feature of ACE-inhibitor therapy?

- **A)** Causes a reduction in intraglomerular pressure
- **B)** Causes relaxation of afferent arterioles of the glomerulus
- **C)** Contraindicated in established diabetic nephropathy
- **D)** Has no effect on microalbuminuria in patients with type 1 diabetes
- **E)** Has no effect on systemic vascular resistance

Answer

Correct answer : Causes a reduction in intraglomerular pressure

ACE inhibitors act by blocking the renin-angiotensin-aldosterone system (RAAS). They are competitive inhibitors of angiotensin converting enzyme (ACE), which catalyse the conversion of the inactive angiotensin I to the powerful vasoconstrictor and stimulator of aldosterone release, angiotensin II. Inhibition of ACE thus results in a decrease in the production of angiotensin II and hence a decrease in vasoconstriction and a decrease in the levels of aldosterone, with resulting reduction in intraglomerular pressure. The result is a decrease in peripheral resistance and a decrease in the retention of salt and water, hence decreasing blood pressure. ACE inhibitors also reduce the breakdown of the potent vasodilator bradykinin. Increased levels of bradykinin may further enhance vasodilation and contribute to blood pressure reduction.

ARBs act by blocking the RAAS further downstream than ACE inhibitors. They block the actions of angiotensin II by competitively binding to the angiotensin type 1 (AT1) receptor. It is via this receptor that angiotensin II normally exerts its effects. These effects are an increase in vasoconstriction leading to increased total peripheral resistance and an increase in the production of aldosterone leading to the retention of salt and water and hence increased blood volume. The result is an increase in blood pressure. By blocking the AT1 receptor, ARBs prevent these effects of angiotensin II and hence decrease blood pressure. As ARBs, unlike ACE inhibitors, do not block the action of the enzyme ACE, they do not inhibit the breakdown of bradykinin. ARBs therefore are not associated with the persistent dry cough often seen with ACE inhibitor therapy.

Direct renin inhibitors, such as aliskiren, act to block the action of renin in converting angiotensinogen to angiotensin I.

Question 25

A 56 year old man with a 5 year history of type 2 diabetes has a Hba1c of 66.1 mmol/mol(8.2%)(42.1 mmol/mol(<6)), a BMI of 36 kg/ m^2 and blood pressure of 155/78 mmHg. His current medication includes metformin 850 mg tds, gliclazide 160 mg bd, simvastatin 20 mg daily, ramipril 5 mg daily and bendrofluazide 2.5 mg daily. Based on current NICE guidelines he is commenced on exenatide at a starting dose of 5µg bd.

Which of the following is a feature of the therapeutic profile of exenatide?

- **A)** Exenatide has over 90% homology to human GLP-1
- **B)** Exenatide undergoes hepatic and renal clearance
- **C)** Exenatide has a terminal half life of 2.5 hours
- **D)** Exenatide treatment causes pancreatitis
- **E)** 20% of patients will develop neutralizing antibodies to exenatide.

Answer

Correct answer : Exenatide has a terminal half life of 2.5 hours

Exenatide is an exendin derived peptide with 53 % homology to human GLP-1 and is consequently resistant to degradation by human DPP-IV. It is predominantly cleared via renal excretion and is therefore not recommended in patients with an eGFR < 30. Exenatide has a half-life of around 2.5 hours and therefore is given twice daily by subcutaneous injection. No causal link between exenatide and pancreatitis has to date been identified, although a higher incidence of pancreatitis has been reported in association with exenatide (0.49 cases per 1000 patient years) compared with the background rate of pancreatitis in the general population (0.44- 0.47 cases per 1000 patient years). Neutralizing antibodies to exenatide have been infrequently identified, with a maximum incidence of around 3%. Anti-exenatide antibodies are however identified in up to 40% of patients, the clinical relevance of this finding is unclear.

Question 26

A publication reports the outcome of a new statin therapy in a placebo controlled primary prevention of ischaemic heart disease in a diabetic population. 1000 patients were randomised to receive the new therapy and 1000 allocated to placebo. The study was completed over a five year period. In the placebo group there were 150 myocardial infarctions and in the group treated with the new statin there were 100 myocardial infarctions. What is the number needed to treat with the new statin versus the placebo to prevent one MI over the course of this study?

- **A)** 10
- **B)** 20
- **C)** 30
- **D)** 40
- **E)** 50

Answer

Correct answer : 20

In the new statin group, there were 100 MIs in 1000 patients treated. In the conventional statin group there were 150 MIs in 1000 treated patients. Therefore treating 1000 patients one would have 50 fewer MIs. Thus the Number needed to treat with the new statin to prevent 1 MI is 1000/50 = 20.

Question 27

A new antiplatelet agent has been proven to reduce the risk of stroke in a year from 10% in patients treated with conventional treatment to 6% in patients treated with conventional treatment plus the new agent. The cost of this new drug is £10 per month extra than conventional therapy.

How much extra would a hospital need to spend per year to prevent one stroke?

- **A)** £1200
- **B)** £3000
- **C)** £4800
- **D)** £6000
- **E)** £12000

Answer

Correct answer : £3000

To answer this question firstly one needs to calculate the number needed to treat to prevent one stroke. In this case the annual number of strokes with the new agent per 100 patients treated is 6 and in the conventional treatment it is 10. Therefore there are 4 fewer strokes per hundred patients treated with the new drug giving an NNT of 25. Therefore, you would need to treat 25 patients for one year to prevent 1 stroke each of which costs an extra £120. Therefore, it would cost the hospital an extra 25 x 120 = £3000 to prevent one stroke with the newer treatment.

Question 28

A 54 year old male attends the diabetic clinic for routine review. He has had diabetes for ten years and is currently receiving metformin 1g bd combined with biphasic insulin – novomix 30. He also takes simvastatin 40 mg daily. Investigations reveal:

		Normal Ranges
HbAIc	87 mmol/mol (10.1%)	(<6)
U+Es	Normal	
Total Cholesterol	5.5 mmol/l	(<5)
hdL	0.8 mmol/l	(0.9 - 1.9)
Triglycerides	4.1	(0.8 - 2.2)
Free T4	12.1 pmol/l	(10 - 22)
TSH	4.8 mu/l	(0.5 - 5)
Thyroid autoantibodies	>1300 iu/l	(<200)/td>
Albumin:creatinine ratio	2.6	(<2.5)

Which of the following is the most likely cause for this patient’s dyslipidaemia?

- **A)** Hypothyroidism
- **B)** Nephrotic syndrome
- **C)** Poor glycaemic control
- **D)** Type III hyperlipidaemia
- **E)** Type V hyperlipidaemia

Answer

Correct answer : Poor glycaemic control

This patient has a typical dyslipidaemia of type 2 diabetes with poor glycaemic control. With a HbA1c above 63.9 mmol/mol (8%) this reflects defective chylomicron metabolism contributing to excess triglyceridaemia and increased cholesterol. Improving glycaemic control by reducing HBA1c by 1% would be expected to reduce triglycerides by up to 0.5 mmol/l. This is not hypothyroidism as TSH levels are normal and the thyroid autoantibodies mean nothing other than a 30% lifetime risk of developing hypothyroidism.

Question 29

A 62 year old male, who has been newly diagnosed with diabetes by his GP, is referred to clinic. He is on a diet, but currently taking no medication. His blood pressure is 136/82 mmHg, his BMI is 32 kg/m^2 and his investigations reveal:

		Normal Ranges
Fasting Plasma Glucose	7.6 mmol/l	(3.5 - 5.5)
HbA1c	49.2 mmol/mol (6.65%)	(<6)
Total Cholesterol	5.0 mmol/l	(<5)
HDL Cholesterol	0.9 mmol/l	(0.9 - 2.2)
Triglycerides	3.3 mmol/l	(0.9 - 2.2)

Which is the most appropriate agent to treat his dyslipidaemia?

- **A)** Atorvastatin
- **B)** Fenofibrate
- **C)** Nicotinic acid
- **D)** Omega-3 fatty acids
- **E)** Weight reduction

Answer

Correct answer : Atorvastatin

Since this patient is over the age of 40 years old and has a normal to high cardiovascular risk for someone with type 2 diabetes, the most appropriate treatment for his elevated cholesterol (target total cholesterol and LDL cholesterol below 4 and 2 respectively) would be a statin. Do not routinely add other agents like fibrates, nicotinic acid or bile acid sequestrants.

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Question 30

A 38 year old Afro-caribbean lady attends diabetic clinic for annual review. She was diagnosed with diabetes 4 years previously and was treated immediately on novomix 30 twice daily due to her presentation with a fasting plasma glucose of 21 mmol/l and osmotic symptoms. Her glycaemic control has been excellent with an HbA1c range of between 36.6 - 47.5 mmol/mol (5.5 – 6.5%). Over the last 12 months her insulin dose requirements have fallen such that she is receiving insulin 4 iu twice daily. Her BMI is 28 kg/m^2.
Investigations reveal:

		Normal Ranges
Fasting Plasma Glucose	3.6 mmol/l	(3.5 - 5.5)
HbAIc	33.3 mmol/mol 5.2%	(<6)
ICA	0.0 iu/l	(<0.1)
GAD antibody	0.01 iu/l	(<0.5)
Triglyceride	0.7 mmol/l	(0.9 - 2.2)
Total Cholesterol	3.5 mmol/l	(<5)

Which of the following is the diagnosis?

- **A)** Type 1 diabetes
- **B)** Type 2 diabetes
- **C)** LADA
- **D)** MODY type 1
- **E)** MODY type 2

Answer

Correct answer : Type 2 diabetes

Afro-Caribbeans may present with type 2 diabetes with marked hyperglycaemia which is particularly sensitive to insulin therapy. The patient should be treated with withdrawal of insulin and commencement of diet modification alone and monitoring.

Question 31

A study embarks on a new method of measuring insulin resistance in a group of obese subjects. It utilises mathematical modelling of certain new serological markers. Which of the following would be the appropriate standard measure of insulin resistance against which this new technique should be compared?

- **A)** Homeostatic model assessment (HOMA)
- **B)** Hyperinsulinaemic euglycaemic clamps
- **C)** Insulin tolerance test
- **D)** Oral glucose tolerance test
- **E)** Quantitative insulin sensitivity check index (QUICKI)

Answer

Correct answer : Hyperinsulinaemic euglycaemic clamps

Hyperinsulinaemic euglycaemic clamp is the gold standard technique against which other techniques, as listed above may be used.

Question 32

A technique of measuring insulin resistance whereby the product of the fasting values of glucose and insulin are divided by a constant of 22.5. To which technique does this description refer?

- **A)** Glucose/insulin ratio (GI ratio)
- **B)** Glycaemic index
- **C)** Homeostatic model assessment (HOMA)
- **D)** Quantitative insulin sensitivity check index (QUICKI)
- **E)** Score for insulin sensitivity index (ISI)

Answer

Correct answer : Homeostatic model assessment (HOMA)

HOMA is one of the most widely used and easiest techniques of measuring insulin sensitivity/ resistance. It generally correlates well with insulin clamp studies.

Question 33

‘Healthy fasted subjects are given a 50g carbohydrate meal and glucose concentrations are measured every 15 mins for the first hour and every 30 mins for up to 2 hours. These glucose concentrations are then compared with values after the consumption of 50g of glucose’.
To which of the following does this methodology refer?

- **A)** Glucose tolerance test
- **B)** Glycaemic load
- **C)** Glycaemic index
- **D)** Prolonged glucose tolerance test
- **E)** The standard meal test

Answer

Correct answer : Glycaemic index

This description of the measurement of glucose concentrations following a specific carbohydrate compared with glucose itself is that of the glycaemic index. High GI index foods have a value of 70 or above, medium 56-69 and low <55.

Question 34

From which of the following is glucagon-like peptide 1 (GLP-1) produced?

- **A)** Body of stomach
- **B)** Ileum
- **C)** Liver
- **D)** Pancreas
- **E)** Pylorus

Answer

Correct answer : Ileum

GLP-1 is a hormone produced by the L-cells of the ileum and has effects on insulin and glucagon secretion by the pancreatic islets, as well as having central effects regulating caloric intake.

Question 35

Which of the following effects are mediated by GLP-1?

- **A)** Delayed gastric emptying time
- **B)** Increased jejunal transit time
- **C)** Increased gastric acid secretion
- **D)** Increased pancreatic exocrine enzyme secretion
- **E)** Increased bile acid secretion

Answer

Correct answer : Delayed gastric emptying time

GLP-1 produces satiety through a number of mechanisms including reduced gastric emptying and is also felt to act through central effects reducing hunger.

Question 36

A 58 year old female is referred by the GP who is concerned about her hyponatraemia. He recently performed U+Es which reveal:

		Normal Ranges
Sodium	124 mmol/l	(134 - 144)
Potassium	3.6 mmol/l	(3.5 - 5)
Urea	5.5 mmol/l	(3 - 8)
Creatinine	90 micromol/l	(50 - 100)
Glucose	9.2 mmol/l	(3.5 - 5.5)
HbA1c	55.2 mmol/mol (7.2%)	(<36.6 mmol/mol (<5.5))

She is generally well and has a history of diabetes, depression and hypertension for which she is receiving gliclazide 80 mg bd, metformin 500 mg tds, Lisinopril 20 mg daily, amlodipine 10 mg daily and citalopram 20 mg daily. Her hyponatraemia is confirmed and the following results are returned:

Urine sodium	44 mmol/l
Urine osmolality	610 nmosmol/l

Which of the following is the likely cause of her hyponantraemia?

- **A)** Citalopram
- **B)** Gliclazide
- **C)** Hypoadrenalism
- **D)** Lisinopril
- **E)** Type IV renal tubular acidosis

Answer

Correct answer : Citalopram

The patient has a hyponatraemia with inappropriate conservation of urine sodium and highish urine osmolality versus a plasma osmolality of approx 269 mosmol/l - Claculated as - 2x (sodium+potassium) + Urea + Glucose. The most likely explanation for this is SIADH and the most likely precipitant of SIADH is Citalopram. SSRIs are a common cause of hyponatraemia due to SIADH. Type IV RTA (hyporeninaemic hypoaldosteronism) is unlikely as this is usually associated with a higher potassium concentration.

Question 37

A 28 year old female presents at 14 weeks into her second pregnancy. She previously gave birth to a healthy baby boy 2 years ago who weighed 4 Kg. The patient has a history of polycystic ovarian syndrome and has previously been treated with metformin to assist with conception. The only other issue of note is that her cousin has type 1 diabetes. She has a BMI of 32.3 kg/m^2 and is otherwise fine.

Which of the following would be a reason for screening this patient for gestational diabetes?

- **A)** Her age
- **B)** Her BMI
- **C)** Her family history of diabetes
- **D)** Her history of polycystic ovarian syndrome
- **E)** The previous weight of her infant

Answer

Correct answer : Her BMI

Screening for gestational diabetes (GDM) is hotly debated with the general acceptance of case selection being advocated. NICE advise testing for GDM in the following scenarios:

- 1st degree relative with diabetes (her cousin is not a first degree relative)
- Previous pregnancy with macrosomia (>4.5kg)
- Previous gestational diabetes
- BMI above 30
- Family origin with a high prevalence of diabetes

Question 38

A 68 year old man has a long history of type 2 diabetes with end stage renal disease. He has had some problems with associated hyperkalaemia and has been advised a low potassium diet.

Which of the following foods should he specifically avoid?

- **A)** Apples
- **B)** Grapefruits
- **C)** Oranges
- **D)** Peaches
- **E)** Pineapple

Answer

Correct answer : Oranges

Hyperkalaemia is a common biochemical abnormality in chronic renal failure and a low potassium diet is frequently required. Foods with a high potassium content which should be avoided include avocado, banana, tomato, oranges, orange juice and potato. Also canned fruits have a high potassium content.

Question 39

A 23 year old type 1 diabetic man has noticed some problems in relation to his postprandial glucose excursions after eating certain foods. He has read about the glycaemic index (GI) of foods and its impact on postprandial glucose concentrations. Which of the following foods has the highest GI value?

- **A)** Apples
- **B)** Baked potatoes
- **C)** Boiled potatoes
- **D)** Peaches
- **E)** Spaghetti

Answer

Correct answer : Baked potatoes

The Glycaemic Index (GI) relates solely to carbohydrates and is a measure of by how quickly a food raises plasma glucose compared with glucose itself. Carbohydrates can be scored from 0 to 100 where glucose has a GI of 100. Thus, the GI index provides information on whether a food raises blood sugar levels dramatically, moderately or minimally - high, moderate or low GI values. Apples, peaches oranges and even chocolate are considered low GI (less than 55). Yet, through different preparation, the GI can alter – mashed potatoes (70) and baked potatoes (85) have a high GI (above 70) whilst boiled potatoes have a moderate GI of 58. Foods only appear if they contain carbohydrate hence meats, eggs and fish do not appear in the GI index. The GI is important in diabetes and conditions related to postprandial hypoglycaemia or dumping syndrome. Generally, the lower the GI index the ‘better’ the carbohydrate.

Question 40

A 52 year old male is seen 6 weeks after being admitted to hospital with an inferior myocardial infarction (MI). He was diagnosed with type 2 diabetes two years ago and was taking metformin 500 mg tds, ramipril 10 mg daily and simvastatin 40 mg daily. He had received thrombolysis and made an uneventful recovery. He was a smoker of 10 cigarettes per day but has since given up. After his MI, he was also prescribed atenolol 25 mg daily and aspirin 75mg daily.

On examination he is well, his blood pressure is 128/78 mmHg and pulse 64 bpm.

Investigations reveal:

		Normal Ranges
Total Cholesterol	3.6 mmol/l	(<5)
HDL	1.5 mmol/l	(0.9-1.9)
Plasma Triglycerides	1.4 mmol/l	(0.9 – 2.2)
HbA1c	54.1 mmol/mol (7.1%)	(<42 mmol/mol (6))

Which of the following is the most appropriate management concerning further cardiovascular risk reduction?

- **A)** Add ezetimibe
- **B)** Add fenofibrate
- **C)** Add niacin
- **D)** No changes required
- **E)** Switch simvastatin to atorvastatin (80 mg)

Answer

Correct answer : Switch simvastatin to atorvastatin (80 mg)

This patient has appropriate cholesterol concentrations with his current statin therapy, yet the GISSI-III study revealed that the use of omega-3 fatty acids in patients following MI treated with all conventional post-MI therapy was associated with a further 25% reduction in cardiovascular mortality.

_____ Secondary prevention 1.3.20 Start statin treatment in people with CVD with atorvastatin 80 mg[6]. Use a lower dose of atorvastatin if any of the following apply: potential drug interactions high risk of adverse effects patient preference. [new 2014] For information about implementing this recommendation, see Implementation: getting started. 1.3.21 Do not delay statin treatment in secondary prevention to manage modifiable risk factors. [2014] 1.3.22 If a person has acute coronary syndrome, do not delay statin treatment. Take a lipid sample on admission and about 3 months after the start of treatment. [2008, amended 2014] https://www.nice.org.uk/guidance/cg181/chapter/1-recommendations#lipid-modification-therapy-for-the-primary-and-secondary-prevention-of-cvd-2

Question 41

A 55 year old male develops muscle aches and pains. He has a history of ischaemic heart disease and has been taking simvastatin for the last 3 years without any particular problems. However, most recently he has started to lead a healthier lifestyle and has been taking some health supplements. Consumption of which of the following supplements may have precipitated this statin-induced myalgia?

- **A)** Cranberry juice
- **B)** Garlic capsules
- **C)** Ginseng
- **D)** Grapefruit juice
- **E)** Vitamin C

Answer

Correct answer : Grapefruit juice

Grapefruit juice is a recognised hepatic enzyme inhibitor and statin-induced myalgia/myositis is described following regular consumption of grapefruit juice.

Question 42

A 41 year old gentleman attends his GP for a routine life insurance medical. He has no past medical history of note and feels generally well. On examination his blood pressure is 155 / 85 mmHG, his BMI is 32 kg / m^2, his waist circumference is 102 cm and his body weight is 98.4 kg.

Investigations reveal:

		Normal Ranges
Fasting Plasma Glucose	5.3 mmol/l	(3.5 - 6)
Total Cholesterol	5.4 mmol/l	(<5.5)
Plasma Triglyceride	2.1 mmol/l	(0.9 - 2.2)
HDL Cholesterol	0.9 mmol/l	(0.9-1.9)
LDL Cholesterol	3.3 mmol/l	(<2)

Based upon the IDF criteria, which of the following would support a diagnosis of the metabolic syndrome in this man?

- **A)** His BMI, triglyceride concentration and fasting glucose
- **B)** His BMI, blood pressure and triglyceride concentration
- **C)** His waist circumference, blood pressure and fasting glucose
- **D)** His waist circumference, blood pressure and HDL concentration
- **E)** His waist circumference, HDL-cholesterol and total cholesterol

Answer

Correct answer : His waist circumference, blood pressure and HDL concentration

This gentleman meets the criteria for metabolic syndrome, as defined by the International Diabetes Federation (IDF), since he has central obesity (waist circumference ≥94 cm), a plasma triglyceride ≥1.7 mmol/l, blood pressure ≥130 / 85 mmHg and a HDL-cholesterol < 1.04 mmol/l.

The IDF definition of the metabolic syndrome is based on the presence of central obesity (waist circumference in Europeans is ≥94 cm in men and ≥80 cm in women) combined with any two of the following:

Plasma Triglyceride	≥1.7 mmol/l
HDL Cholesterol	< 1.04 (Men)
HDL Cholesterol	< 1.29 (Women)
Fasting Plasma Glucose	≥ 5.5 mmol/l
Blood Pressure	≥ 130/85 mmHg or receiving Anti-hypertensive Treatment

Reference:
https://www.idf.org/our-activities/advocacy-awareness/resources-and-tools/60:idfconsensus-worldwide-definitionof-the-metabolic-syndrome.html

Question 43

A 49 year old man attends the medical outpatient clinic for review of his blood pressure control. His current medication includes perindopril 8 mg daily, amlodipine 5 mg daily and doxazosin 4 mg daily. On examination, his blood pressure is 156 / 88 mm Hg, his BMI is 34 kg / m^2 and his waist circumference is 96 cm.

		Normal Ranges
Fasting Plasma Glucose	5.4 mmol/l	(3.5 - 6)
Total Cholesterol	4.6 mmol/l	(<5.5)
Plasma Triglycerides	1.8 mmol/l	(0.9 - 2.2)
HDL Cholesterol	0.8 mmol/l	(0.9 - 1.9)
LDL Cholesterol	3.2 mmol/l	(< 3)

Which of the following criteria would suggest a diagnosis of metabolic syndrome in this gentleman according to the International Diabetes Federation?

- **A)** BMI, LDL-C concentration and blood pressure
- **B)** BMI, fasting plasma glucose and plasma triglyceride concentration
- **C)** Waist circumference, HDL-cholesterol concentration and blood pressure
- **D)** Waist circumference, triglyceride concentration and LDL-cholesterol concentration
- **E)** Waist circumference, HDL-cholesterol and LDL-cholesterol concentration

Answer

Correct answer : Waist circumference, HDL-cholesterol concentration and blood pressure

This gentleman meets the criteria for metabolic syndrome, as defined by the International Diabetes Federation, since he has central obesity (waist circumference ≥94 cm), a plasma triglyceride ≥1.7 mmol/l, blood pressure ≥130 / 85 mmHg and a HDL-cholesterol < 1.04 mmol/l. The IDF definition of the metabolic syndrome is based on the presence of central obesity (waist circumference in Europeans is ≥94 cm in men and ≥80 cm in women) combined with any two of the following:

Plasma Triglyceride	≥1.7 mmol/l
HDL Cholesterol	< 1.04 (Men)
HDL Cholesterol	< 1.29 (Women)
Fasting Plasma Glucose	≥ 5.6 mmol/l
Blood Pressure	≥ 130/85 mmHg or receiving Anti-hypertensive Treatment

Reference
https://www.idf.org/our-activities/advocacy-awareness/resources-and-tools/60:idfconsensus-worldwide-definitionof-the-metabolic-syndrome.html

Question 44

A 24 year old lady with an 8 year history of type 1 diabetes attends antenatal clinic, with her first pregnancy at 10 weeks gestation. Her pre-conception Hba1c was 66.1 mmol/mol (8.2%)(<42.1 mmol/mol(6)) and her current medication includes novomix 30 32 units in the morning and 34 units in the evening. She is subsequently converted to a basal bolus insulin regimen comprising of novorapid and levemir at an initial total daily dose of 74 units. Subsequent dose modifications are conducted on the basis of continuous glucose monitoring (CGM)

Which of the following is associated with the use of CGM during pregnancy?

- **A)** Reduced risk of fetal trisomy 21
- **B)** Reduced risk of neural tube defects
- **C)** Reduced risk of shoulder dystocia
- **D)** Reduced risk of fetal malformation
- **E)** Reduced risk of neonatal hypoglycaemia

Answer

Correct answer : Reduced risk of shoulder dystocia

A recent study has suggested that CGM improves glucose control in the third trimester of pregnancy, leading to decreased mean birth weight, thus reducing the incidence of macrosomia and hence shoulder dystocia which is a common problem with macrosomic babies.

CGM in pregnancy

Question 45

A 78 year old man attends clinic for review. He has a 5 year history of type 2 diabetes and his current medication includes metformin 1 gram twice daily, perindopril 4 mg daily and Aspirin 75 mg once daily. He has a past history hypertension and was admitted to hospital 3 years previously with congestive heart failure. On examination, his BMI is 31 kg/m^2, his blood pressure is 166/86 mmHg, cardiovascular and respiratory system examinations are both normal. He feels generally well although complains of feeling tired and gets up at least twice a night to pass water. He is self-caring, independent and has normal cognitive function.

		Normal Ranges
Haemoglobin	13.1 g dl	(11 - 16)
Hba1c	71.6 mmol/mol (8.7%)	(<42.1 mmol/mol(6))
Total Cholesterol	4.4 mmol/l	(<5)
Plasma Triglyceride	2.1 mmol/l	(0.9 - 2.2)
TSH	1.35 mu / l	(0.32 - 5.5)
eGFR	53 ml/min/1.73m²	

In accordance with NICE guidelines, which of the following would be the most appropriate management with respect to this man's glycaemic control?

- **A)** Add gliclazide 80 mg once a day
- **B)** Add pioglitazone 30 mg once daily
- **C)** Increase metformin dose
- **D)** No other intervention required
- **E)** Start once daily insulin glargine

Answer

Correct answer : Add gliclazide 80 mg once a day

This man has poor glucose control with associated symptoms. According to current NICE guidance a sulphonylurea would be the most appropriate additional therapy . There is no role for increasing metformin further. SGLT2 inhibitors are also good a choice as a second line treatment if weight loss is intended and effective to reduce heart failure. He is not a candidate for pioglitazone since he has a previous history of heart failure, even though there is no current clinical evidence of heart failure.

Management of Type 2 diabetes

Question 46

The following description summarizes a standardized technique outlined in a research proposal that you are submitting for local ethical approval:

"Through a peripheral vein, insulin is infused at 10-120 mU per m^2 per minute. Glucose 20% is infused to maintain blood sugar levels between 5 and 5.5 mmol/l. The rate of glucose infusion is determined by checking the blood glucose levels every 5 to 10 minutes. The rate of glucose infusion during the last 30 minutes of the test determines insulin sensitivity. If high levels (7.5 mg/min or higher) are required, the patient is insulin-sensitive. Very low levels (4.0 mg/min or lower) indicate insulin resistance. Levels between 4.0 and 7.5 mg/min are not definitive and suggest impaired glucose tolerance."

Which of the following methodologies is outlined above?

- **A)** Homeostatic Model Assessment (HOMA)
- **B)** Hyperinsulinaemic euglycaemic clamp
- **C)** Intravenous glucose tolerance test
- **D)** Quantitative insulin sensitivity check index
- **E)** Hyperglycaemic clamp

Answer

Correct answer : Hyperinsulinaemic euglycaemic clamp

This is the classical example of the hyperinsulinaemic euglycaemic clamp used as the gold standard to assess insulin sensitivity. Clamp techniques are relied upon in research studies as well as phase 3 and 4 interventions to assess the impact of pharmacological agents and interventions impact on insulin sensitivity.

Question 47

A 48 year old Asian lady is referred to the diabetes clinic. She has a 4 year history of type 2 diabetes and speaks very little English. Her current medication includes metformin 1 gram twice daily, gliclazide 160 mg twice daily, lisinopril 10 mg daily and simvastatin 20 mg daily. On examination, her BMI is 28 kg/m^2, her body weight is 71 kg and her blood pressure is 136/76 mmHg.
Investigations reveal:

		Normal Ranges
Hba1c	66.1 mmol/mol (8.2%)	(<42.1 mmol/mol (6))
Total Cholesterol	4.4 mmol/l	(<5)
Plasma Triglyceride	1.8 mmol/l	(0.9 - 2.2)
Thyroid Function Tests	Normal	
eGFR	62 ml/min/1.73m²	(90-110)

Which of the following patient education programmes would be the most appropriate for this lady?

- **A)** BERTIE
- **B)** Conversation mapping
- **C)** DAFNE
- **D)** DESMOND
- **E)** EXPERT

Answer

Correct answer : Conversation mapping

Conversation mapping would be the most appropriate for this lady, as it is a primarily visually based patient education course and as such it can be effectively delivered with the support of interpreters. It is probably the most useful of the listed educational techniques for patients with limited English speaking capacity.http://www.diabetesforecast.org/2018/02-mar-apr/conversation-maps-aid.html

Question 48

A 27 year old lady with a 5 year history of type 1 diabetes is seen in the clinic. She is generally well and expresses a wish to be referred to a structured education programme as a means of improving her blood glucose control. On examination her BMI is 25 kg/m^2, her body weight is 68 kg and her blood pressure is 125/75 mmHg. Her current medication includes novorapid and levemir at a total daily dose of 84 units.
Investigations reveal:

		Normal Ranges
Hba1c	73.8 mmol/mol (8.9%)	(<42.1 mmol/mol (6))
Total Cholesterol	4.1 mmol/l	(<4)
Plasma Triglyceride	1.1 mmol/l	(0.9 - 2.2)
Thyroid Function	Normal	

Which of the following structured patient education programmes would be the most appropriate for this lady?

- **A)** BERTIE
- **B)** Conversation mapping
- **C)** DAFNE
- **D)** DESMOND
- **E)** EXPERT

Answer

Correct answer : DAFNE

The DAFNE (Dose Adjustment For Normal Eating) patient education programme is designed for people with type 1 diabetes. It is a course running over 5 consecutive days primarily focusing on diet composition and insulin dose changes.

Question 49

A 56 year old man is admitted to hospital with a lower respiratory tract infection. He is noted on admission to have a random plasma glucose of 15.6 mmol/l (3.5-5.5). He is treated with oral antibiotic therapy, 3 months following his discharge he undergoes a 75 gram oral glucose tolerance test, the results of which are outlined below:

		Normal Ranges
Fasting plasma glucose	7.5 mmol/l	(< 5.6)
2-hour post challenge plasma glucose	13.1 mmol/l	(<11.1)

Which of the following education programmes would be most appropriate for this man?

- **A)** BERTIE
- **B)** Conversation mapping
- **C)** DAFNE
- **D)** DESMOND
- **E)** X-PERT

Answer

Correct answer : DESMOND

This man has a new diagnosis of type 2 diabetes based on his oral glucose tolerance test. The DESMOND education programme is a foundation course for people newly diagnosed with type 2 diabetes and comprises 2 half days over a two week period. X-pert is a programme for either type 1 or type 2's requiring insulin. DAFNE and BERTIE are also for type 1 patients.

Question 50

A 61 year old man with a 6 year history of type 2 diabetes is reviewed in the clinic. On examination his blood pressure is 155/81 mmHg, his BMI is 32 kg/m^2 and his body weight is 86 kg. His current medication includes metformin 1 g twice daily, gliclazide 160 mg twice daily, atorvastatin 20 mg daily, enalapril 20 mg once daily and amlodipine 5 mg once daily. His most recent Hba1c is 76.0 mmol/mol (9.1%) (<42.1 mmol/mol (6)) so you decide to commence a once daily insulin analogue.

Which of the following patient education programmes would be the most appropriate for this man?

- **A)** BERTIE
- **B)** Conversation mapping
- **C)** DAFNE
- **D)** DESMOND
- **E)** X-PERT

Answer

Correct answer : X-PERT

The X-PERT patient education programme is primarily designed for patients with relatively recently diagnosed type 2 diabetes. It is also however, suitable for patients with type 2 diabetes of longer duration and in particular patients with type 2 diabetes commencing on insulin.

Question 51

You have established a research project to assess the effect of dietary conjugated linoleic acid supplementation on beta cell function in people with treatment naive type 2 diabetes.
Which of the following is the most appropriate method of assessing first phase insulin secretion?

- **A)** 100 gram oral glucose tolerance test
- **B)** Frequently sampled IV glucose tolerance test (FSIVGTT)
- **C)** Hyperinsulinaemic euglycaemic clamp
- **D)** HOMA beta estimation
- **E)** 4 hour mixed meal tolerance test

Answer

Correct answer : Frequently sampled IV glucose tolerance test (FSIVGTT)

The FSIVGTT allows for very rapid collection of blood for insulin estimation during the early period following glucose injection. First phase insulin secretion is defective early in the natural history of type 2 diabetes, while the restoration of early phase insulin secretion may be a feature if improved beta cell function.

Question 52

A 69 year old woman undergoes a right hemicolectomy for ulcerative colitis. She has a 5 year history of type 2 diabetes with her pre-operative medication including metformin 500 mg three tds, pioglitazone 30 mg od and gliclazide 80 mg bd, with her preoperative Hba1c being 58.5 mmol/mol (7.5%) (<42.1 mmol/mol (6)). The surgical procedure is successful and the immediate postoperative period unremarkable, during which time she has been managed with intravenous variable rate insulin infusion (VRII). Her appetite remains poor and the surgical team is concerned with respect to her nutritional status since at one week post surgery she is noticed to have lost 4.4 kg in weight compared to her admission body weight. She is consequently commenced on an 18 hour enteral feeding regimen.
Which of the following is the most appropriate method of managing this lady's blood glucose during this period?

- **A)** Continue with intravenous sliding scale insulin
- **B)** Commence subcutaneous sliding scale insulin
- **C)** Introduce subcutaneous basal insulin regimen
- **D)** Introduce a subcutaneous GLP-1 analogue
- **E)** Re-introduce gliclazide in association with her enteral feed

Answer

Correct answer : Introduce subcutaneous basal insulin regimen

According to the JBDS guidelines 2012:

Maintaining euglycaemia in patients receiving enteral feeding is often challenging. Aim to keep blood glucose with in target range 6-12 mmol/L

Carbohydrate in enteral feeds is often absorbed quickly leading to hyperglycaemia and so insulin requirements often increase.

The catabolic state that occurs after major surgery and the patient's poor nutritional state mean it is important to achieve good glucose control.

It is often impractical to use intravenous insulin for a prolonged period of time and so a simple subcutaneous regimen using basal insulin is often preferred.

Question 53

A 39 year old gentleman is referred to clinic for review. He has a 2 year history of type 2 diabetes and his current medication includes metformin 1 gram twice daily, perindopril 8 mg daily and simvastatin 40 mg daily. He was also taking pioglitazone 30 mg daily, but discontinued this 4 months ago due to progressive weight gain; he has also been intolerant of orlistat due to abdominal discomfort and diarrhoea. On examination, his BMI is 43 kg/m^2 and his blood pressure is 166/88 mmHg.
Investigations reveal:

		Normal ranges
Hba1c	73.8 mmol/mol (8.9%)	(<42.1 mmol/mol (6))
Total cholesterol	4.9 mmol/l	(<5)
Plasma triglyceride	3.1 mmol/l	(0.9 - 2.2)
TFTs	Normal	

Which of the following treatments is associated with the greatest reduction in future morbidity/ mortality for this man?

- **A)** Bariatric surgery
- **B)** Gliclazide 80 mg twice daily
- **C)** Exenatide 5 micrograms twice daily
- **D)** Sitagliptin 100 mg once daily
- **E)** Pioglitazone 30 mg daily

Answer

Correct answer : Bariatric surgery

Data from the Swedish obesity study coupled with long term follow up data post-bariatrioc surgery have demonstrated diabetes remission in up to 70% of patients at 5 years following bariatric surgery, with up to 40 % of patients demonstrating remission of diabetes at 10 years post surgery. These observations are coupled with a 29% reduction in all cause mortality associated with 16 – 25% excess weight loss at 10 years post bariatric surgery, along with a 92% reduction in diabetes related mortality.

Question 54

You are contacted by a cardiology SpR to a review a 64 year old man who was recently admitted with an episode of troponin positive chest pain. He has a 7 year history of type 2 diabetes and his current medication includes metformin 1 gram twice daily, gliclazide 160 mg twice daily, Warfarin as per INR, atorvastatin 40 mg daily, perindopril 4 mg daily and bisoprolol 5 mg daily.

On examination his blood pressure is 155/75 mmHg, his BMI is 38 kg/m^2 and he has no evidence of cardiac failure. The cardiology team are thus considering the possibility of exenatide, but are unsure of the any specific contraindications.

Further investigations reveal:

		Normal Ranges
Hba1c	73.8 mmol/mol (8.9%)	(<42.1 mmol/mol (6))
Total Cholesterol	4.9 mmol/l	(<5)
Plasma Triglyceride	3.9 mmol/l	(0.9 - 2.2)
eGFR	55 $ml/min/1.73m^2$	(90-110)

Trans thoracic echo LV ejection fraction of 35% with an LV mural thrombus

Which of the following is a specific contraindication to exenatide therapy?

- **A)** Concomitant Warfarin therapy
- **B)** LV ejection fraction < 30%
- **C)** Type III hyperlipoproteinaemia
- **D)** Type V hyperlipoproteinaemia
- **E)** eGFR < 30 m l / min /1.73 m2

Answer

Correct answer : eGFR < 30 m l / min /1.73 m2

Exenatide is contraindicated in people with significant renal impairment. Exenatide has no direct drug interaction with warfarin, but may impact on INR through affecting warfarin absorption due to delayed gastric emptying. Exenatide is associated with an increased incidence of reported pancreatitis, but hypertriglyceridaemia (also a risk factor for pancreatitis) is not a contraindication to exenatide. There is limited experience with exenatide, although no specific contraindication exists, however, GLP-1 has been shown to exert beneficial effects on left ventricular function.

Reference:

Renal failure and exenatide

Question 55

A 56 year old man with a body mass index of 34 kg/m^2 is found to have a random plasma glucose of 12.1 mmol/l during a recent admission to hospital with a lower respiratory tract infection. One month later he has his fasting plasma glucose measured on two occasions over a 5 day period revealing fasting plasma glucose levels of 6.7 mmol/l and 6.9 mmol/l respectively.

Which of the following would be the most appropriate approach regarding this patient's glucose concentrations?

- **A)** Arrange oral glucose tolerance test
- **B)** Measure HbA1c
- **C)** No further investigation required
- **D)** Repeat fasting glucose in three months
- **E)** Repeat fasting glucose in six months

Answer

Correct answer : Arrange oral glucose tolerance test

This man has, by definition, impaired fasting glucose (IFG) (glucose between 6.1-6.9) and initial management includes lifestyle modification. IFG also has a high incident risk of type 2 diabetes and patients should undergo an oral glucose tolerance test as up to 30% will have overt diabetes.

Question 56

A 65 year old man with a 6 year history of type 2 diabetes is reviewed in clinic. His current medication includes metformin 850 mg twice daily, gliclazide 80 mg twice daily, rosuvastatin 10 mg once daily and perindopril 2 mg a day. On examination, his blood pressure is 156/86 mmHg and his BMI is 33 kg/m^2. Urinalysis reveals 3+ protein and 1+ glucose and a 24 hour urinary collection is subsequently arranged.

Which of the following urine albumin concentrations signifies overt proteinuria?

- **A)** 20 mg / 24 hours
- **B)** 50 mg / 24 hours
- **C)** 100 mg / 24 hours
- **D)** 1 gram / 24 hours
- **E)** 300 mg / 24 hours

Answer

Correct answer : 300 mg / 24 hours

Microalbuminuria = Urine albumin: 20-200 mg/g creatinine (men); 30-300 mg/g creatinine (women).

Overt albuminuria = Urine albumin: >300 mg/day.

Overt proteinuria = Urine total protein: =300 mg/day.

Nephrotic range proteinuria = Urine total protein: =3.5 g/day; Serum albumin: <3.0>

Reference:

BMJ best practice: Proteinuria

Question 57

A 25 year old final year medical student with a 10 year history of type 1 diabetes is reviewed in clinic 4 months following conversion from a basal bolus insulin regimen to an insulin pump. His frequent nocturnal hypoglycaemic episodes have stopped and his Hba1c is now 67 mmol/mol (8.3%). On review of his dietary history he has his main evening meal between 8 and 9 pm, has a light breakfast at around 7 pm, a light lunch at around 1 pm and frequently has a bedtime snack. Continuous glucose monitoring reveals glucose levels of between 7 and 14 mmol/l between 5 and 8 am, with no evidence of hypoglycaemia.

Which of the following is the most appropriate approach to improving this young man's glucose control?

- **A)** Administer correction bolus at 7am
- **B)** Increase basal insulin rate between 11pm and 8am
- **C)** Increase basal rate between 5am and 8am
- **D)** Increase basal rate between 6pm and 11pm
- **E)** Omit bedtime snack

Answer

Correct answer : Increase basal rate between 5am and 8am

This man's glucose profile is typical of the dawn phenomenon with progressive increase in early morning plasma glucose levels in the absence of nocturnal hypoglycaemia. This phenomenon is primarily related to hepatic gluconeogenesis and glycogenolysis, hence the correct management would be to increase the basal insulin infusion rate during this period in order to suppress hepatic glucose release.

Question 58

A GP colleague contacts you regarding referral of patients to the X-PERT patient programme which has been recently commenced by your diabetes service.

Which of the following patients would be the most appropriate to refer to this patient education programme?

HbA1c Normal range less than 42 mmol/mol or 6%

- **A)** A 15 year old girl with a 3 year history of type 1 diabetes, taking a basal bolus insulin regimen with a most recent HbA1c of 67 mmol/mol (8.3 %)
- **B)** A 58 year old man with a 2 year history of type 2 diabetes taking metformin 1 gram twice daily with a most recent HbA1c of 57 mmol/mol (7.4%)
- **C)** A 33 year old man with a 12 year history of type 1 diabetes taking twice daily biphasic insulin with a most recent HbA1c of 73 mmol/mol (8.8%)
- **D)** A 48 year old man with a 3 year history of type 2 diabetes secondary to Pancreatitis taking biphasic insulin with a most recent HbA1c of 61 mmol/mol (7.7%)
- **E)** A 61 year old man with a recent diagnosis of impaired glucose tolerance following a 75 gram oral glucose tolerance test.

Answer

Correct answer : A 58 year old man with a 2 year history of type 2 diabetes taking metformin 1 gram twice daily with a most recent HbA1c of 57 mmol/mol (7.4%)

The X-PERT (and DESMOND) patient programme is 6 week educational programme specifically designed for patients with type 2 diabetes. It has been shown to be effective in improving a number of parameters in diabetes care in trained individuals.

Question 59

A 55 year old Asian lady with a 5 year history of type 2 diabetes is reviewed in clinic. Her current medication includes metformin 1 gram twice daily, pioglitazone 30 mg once daily, simvastatin 20 mg once daily and perindopril 4 mg once daily. On examination her blood pressure is 144/78 mmHg, her BMI is 36.8 Kg/m^2 and her body weight is 75.8 kg. She is a devout Muslim and wishes to fast during daylight hours during the month of Ramadan. Investigations reveal

		Normal Ranges
Hba1c	70.5 mmol/mol (8.6%)	(<42.1 mmol/mol (6))
Total Cholesterol	4.7 mmol/l	(<5)
Plasma Triglyceride	2.1 mmol/l	(0.9 -2.2)
TSH	1.7 mu/l	(0.32 - 5.5)
eGFR	68 ml/min/1.73m²	(90-110)

Which of the following is the most appropriate approach to improve this lady's blood glucose control?

- **A)** Commence SGLT2 inhibitors
- **B)** Commence sitagliptin
- **C)** Commence once daily gliclazide
- **D)** Commence once daily Insulin glargine
- **E)** Commence once daily biphasic insulin

Answer

Correct answer : Commence sitagliptin

This lady is at an increased risk of hypoglycaemia during the month of Ramadan, therefore glucose independent insulin providing therapies such as exogenous insulin and sulphonylureas do not represent the most appropriate treatment option. Exenatide’s mechanism of action utilises the incretin effect, resulting in glucose dependent stimulation of beta cell insulin release and would thus be associated with a reduced risk of hypoglycaemia, particularly in the absence of concomitant sulphonylurea therapy. Exenatide is however associated with appetite suppression and is therefore not acceptable during Ramadan. Sitagliptin is a DPPIV-enzyme inhibitor and thus also utilises the incretin effect to produce glucose reduction, but does not have an effect on appetite suppression and is thus acceptable.

Question 60

A 17 year old young man is reviewed in the adolescent clinic. He has a five year history of type 1 diabetes managed with a basal bolus insulin regimen at a total daily dose of 62 units / day and a most recent Hba1c of 65.0 mmol/mol (8.1%) (<42.1 mmol/mol(6)). He is planning a major night out with his friends to celebrate his 18th birthday and requests some advice on the effect of alcohol on his diabetes management.

Which of the following is the most appropriate advice for this young man?

- **A)** Alcohol increases blood glucose levels and insulin doses should be increased
- **B)** Alcohol produces reductions in blood glucose in the short term so that insulin doses should be reduced
- **C)** Alcohol reduces blood glucose levels for several hours after and insulin doses should be 75%
- **D)** Spirits have less effect on blood glucose than beer
- **E)** Alcohol produces reductions in blood glucose levels for several hours after drinking. A pre-bed meal is advised in conjunction with a modest reduction in insulin dose

Answer

Correct answer : Alcohol produces reductions in blood glucose levels for several hours after drinking. A pre-bed meal is advised in conjunction with a modest reduction in insulin dose

Alcohol produces short term elevations in blood glucose followed by longer term reduction in blood glucose levels after drinking. It is therefore important to advise patients of this possibility and the need for pre-bed food in conjunction with a modest dose reduction following drinking.

Question 61

A 20 year old young man is reviewed in the young adult diabetes clinic. He has a 7 year history of type 1 diabetes and is currently taking a basal bolus insulin regimen comprised of once daily insulin detemir at night combined with preprandial novorapid at a total daily insulin dose of 82 units.

On examination his body weight is 88 kg, his BMI is 28 kg / m^2 and his blood pressure is 110 / 70 mmHg. His most recent Hba1c was 65 mmol/mol (8.1%) (<6) and his main current concern is how to optimally manage his diabetes in relationship to his sporting activities, since he is a keen rugby player having recently been included in the national under 21 squad. As his level of exercise has increased, he has noticed increased variability in his blood glucose profile and an increased frequency of both elevated and low blood sugars, which is starting to adversely affect his athletic performance.

Which of the following is the most appropriate advice for this young man?

- **A)** Consume energy drinks immediately before and during exercise
- **B)** Increase his dose of prandial insulin with his meal following playing rugby to facilitate normalisation of elevated blood glucose levels which may have occurred as a consequence of exercise
- **C)** Omit his dose of prandial insulin with his meal prior exercise or playing a rugby game, while increasing his basal insulin dose on the evening following playing rugby a game of rugby
- **D)** Reduce his dose of basal insulin on the evening following playing a game of rugby and also reduce his dose of prandial insulin with his meal prior to playing rugby
- **E)** Reduce his dose of basal insulin on the evening before he plays a rugby game

Answer

Correct answer : Reduce his dose of basal insulin on the evening following playing a game of rugby and also reduce his dose of prandial insulin with his meal prior to playing rugby

Strenuous exercise such as that related to playing rugby is associated with a depletion in glycogen stores which may result in hypoglycaemia and glucose variability following strenuous exercise. Omitting prandial insulin, or the consumption of energy drinks will result in hyperglycaemia which may adversely affect sporting performance. The optimal approach to managing this young man’s glucose profile would be to modestly reduce his preprandial and post exercise insulin doses on a match day in order to minimise hypoglycaemia risk, while advising a meal containing complex carbohydrates 2-4 hours prior to playing a match.

Question 62

A 27 year old lady attends clinic for review. She has a 10 year history of type 1 diabetes and her current insulin regimen includes once daily insulin glargine at a dose of 34 units at night along with variable doses of preprandial novorapid. Her most recent Hba1c is 57 mmol/mol (7.4%) (<6), but she is keen to achieve an HbA1c of < 48 mmol/mol (6.5%) prior to attempting to conceive since during a first unplanned pregnancy 2 years previously she had experienced a miscarriage which she attributed to her poor blood glucose control at that time. She conducts regular blood glucose monitoring and is motivated to modify her insulin doses according to her blood glucose profile.

Which of the following is the most appropriate advice for this lady in order to achieve a reduction in her Hba1c?

- **A)** Focus on reducing fasting blood glucose levels
- **B)** Focus on reducing pre-meal blood glucose levels
- **C)** Focus on reducing 2 hour postprandial blood glucose levels
- **D)** Focus on reducing pre-bed blood glucose levels
- **E)** Focus on reducing pre bed and fasting blood glucose levels

Answer

Correct answer : Focus on reducing 2 hour postprandial blood glucose levels

At Hba1c concentrations < 58.5 mmol/mol (7.5%), postprandial glucose levels become a more important determinant of Hba1c than fasting or pre-meal blood glucose levels, thus targeting postprandial blood glucose levels to < 8.5 mmol/l would be the optimal approach to improving this lady's glucose control based on her current Hba1c level.

Question 63

A 38 year old man is referred to you for assessment following his recent diagnosis of diabetes, based on two fasting plasma glucose levels of 7.9 mmol/l and 8.1 mmol/l. On examination his blood pressure is 146/76 mmHg, his BMI is 31 kg /m^2 , his body weight is 90 kg and his waist circumference is 97 cm. He is currently receiving no medication; he is a non-smoker and drinks alcohol infrequently. He has no family history of note and his main complaint is that of feeling a little lethargic with some loss of libido.

		Normal Ranges
HbA1c	50.8 mmol/mol (6.8%)	(<42 mmol/mol (6))
Total Cholesterol	4.2 mmol/l	(<5)
Plasma Triglyceride	1.5 mmol/l	(0.9 - 2.2)
TSH	0.98 mu/l	(0.32 - 5.5)
Testosterone	8.1 nmol/l	(9 - 30)
Prolactin	175 mu/l	(50-450)
AST	92 iu/l	(5-40)
Alkaline Phosphatase	295 iu/l	(50-110)

Which of the following is the most appropriate investigation for this gentleman?

- **A)** Islet cell antibody serology
- **B)** GAD antibody serology
- **C)** Serum ferritin
- **D)** Transferrin saturation
- **E)** Overnight dexamethasone suppression test

Answer

Correct answer : Transferrin saturation

This gentleman is likely to have haemochromatosis based on the clinical features of diabetes, deranged liver function tests and low testosterone levels. The diagnosis of haemochromatosis is often made following the incidental finding on routine blood screening of elevated serum liver enzymes. Arthropathy with stiff joints, diabetes, or fatigue, may be the presenting complaint. Other presenting features may include hypogonadism, erectile dysfunction and loss of libido. Serum transferrin and transferrin saturation are commonly used as screening for haemochromatosis. Transferrin binds iron and is responsible for iron transport in the blood. Measuring transferrin provides a crude measure of iron stores, saturation values in excess of 45% are recognized as a threshold for further evaluation of haemochromatosis. Transferrin saturation greater than 62% is suggestive of homozygosity for mutations in the HFE gene. Ferritin, a protein synthesized by the liver is the primary form of iron storage within cells and tissues. Measuring ferritin provides another crude estimate of whole body iron stores though many conditions notably inflammation can elevate serum ferritin. Serum ferritin in excess of 1000 ng/ml is almost always attributable to haemochromatosis.

Question 64

A 52 year old man has been recently diagnosed with type 2 diabetes. He is currently managed with diet and lifestyle modification. On examination his blood pressure is 144 / 75 mmHg, his BMI is 33 kg / m^2, his body weight is 93 kg and his waist circumference is 102 cm. He has just completed the EXPERT patient education program and his most recent Hba1c is 49.7 mmol/mol (6.7%) (<42.1 mmol/mol (6)). On review in the clinic he is well but requests some further information relating to the glycaemic index of food to the management of his diabetes.
Which of the following is the most appropriate advice relating to glycaemic index for this gentleman?

- **A)** Addition of vinegar will increase the glycaemic index
- **B)** The glycaemic index is a measure of insulin response to food ingestion
- **C)** A baked potato is an example of a low glycaemic index food
- **D)** Low glycaemic index foods characteristically have a low carbohydrate content.
- **E)** Low glycaemic index foods are associated with slower rates of carbohydrate digestion and greater hepatic and peripheral tissue carbohydrate extraction.

Answer

Correct answer : Low glycaemic index foods are associated with slower rates of carbohydrate digestion and greater hepatic and peripheral tissue carbohydrate extraction.

The Glycaemic index or GI is a measure of the effects of carbohydrates on blood glucose levels. Carbohydrates that break down rapidly during digestion releasing glucose rapidly into the bloodstream and have a high GI; carbohydrates that break down slowly, releasing glucose gradually into the bloodstream, have a low GI. For most people, foods with a low GI have significant health benefits. The concept was developed by Dr. David J. Jenkins and colleagues in 1980–1981.

A lower glycaemic index suggests slower rates of digestion and absorption of the foods' carbohydrates and may also indicate greater extraction from the liver and periphery of the products of carbohydrate digestion. A lower glycaemic response is often thought to equate to a lower insulin demand, better long-term blood glucose control and a reduction in blood lipids. The insulin index may therefore also be useful as it provides a direct measure of the insulin response to a food.

The glycaemic index of a food is defined as the area under the two hour blood glucose response curve (AUC) following the ingestion of a fixed portion of carbohydrate (usually 50 g). The AUC of the test food is divided by the AUC of the standard (either glucose or white bread, giving two different definitions) and multiplied by 100.

The average GI value is calculated from data collected in 10 human subjects. Both the standard and test food must contain an equal amount of available carbohydrate. The result gives a relative ranking for each tested food.

The current validated methods use glucose as the reference food, giving it a glycaemic index value of 100 by definition. This has the advantages that it is universal and it results in maximum GI values of approximately 100. White bread can also be used as a reference food, giving a different set of GI values (if white bread = 100, then glucose ≈ 140). For people whose staple carbohydrate source is white bread, this has the advantage of conveying directly whether replacement of the dietary staple with a different food would result in faster or slower blood glucose response. The disadvantages with this system are that the reference food is not well-defined, and the GI scale is culture dependent. A low GI food will release glucose more slowly and steadily. A high GI food causes a more rapid rise in blood glucose levels and is suitable for energy recovery after endurance exercise or for a person with diabetes experiencing hypoglycaemia.

The glycaemic effect of foods depends on a number of factors such as the type of starch

(amylose vs amylopectin), physical entrapment of the starch molecules within the food, fat and protein content of the food and organic acids or their salts in the meal — adding vinegar for example, will lower the GI. The presence of fat or soluble dietary fibre can slow the gastric emptying rate thus lowering the GI. Unrefined breads with higher amounts of fibre generally have a lower GI value than white breads. Many brown breads, however, are treated with enzymes to soften the crust, which makes the starch more accessible (high GI).

While adding butter or oil will lower the GI of a meal, the GI ranking does not change. That is, with or without additions, there is still a higher blood glucose curve after white bread than after a low GI bread.

The glycaemic index can only be applied to foods with reasonable carbohydrate content, as the test relies on subjects consuming enough of the test food to yield about 50 g of available carbohydrate. Many fruits and vegetables (but not potatoes) contain very little carbohydrate per serving and thus the GI is negligible. This also applies to carrots, which were originally and incorrectly reported as having a high GI. Alcoholic beverages have been reported to have low GI values, but it should be noted that beer has a moderate GI. Recent studies have shown that the consumption of an alcoholic drink prior to a meal reduces the GI of the meal by approximately 15%. Moderate alcohol consumption more than 12 hours prior to a test does not affect the GI

The GI concept has been criticized for a variety of reasons –

- The glycaemic index does not take into account other factors besides glycaemic response, such as insulin response, which is measured by the insulin index and can be more appropriate in representing the effects from some food content other than carbohydrates.
- The glycaemic index is significantly altered by the type of food, its ripeness, processing, the length of storage, cooking methods, and its variety (white potatoes are a notable example, ranging from moderate to very high GI even within the same variety)
- The glycaemic response is different from one person to another, and even in the same person from day to day, depending on blood glucose levels, insulin resistance, and other factors.
- High-glycaemic-index foods may have a low carbohydrate content, and low-glycaemic-index foods may have a high carbohydrate content. This criticism can be addressed by taking into account the glycaemic load
- Low GI foods (GI range <55) include most fruit and vegetables (except potatoes, watermelon), grainy breads, pasta, legumes/pulses, milk, products extremely low in carbohydrates (fish, eggs, meat, nuts, oils), brown rice
- Medium GI foods (GI range 55 – 69) include whole wheat products, basmati rice, sweet potato, table sugar, most white rices (eg, jasmine).

- High GI foods (GI range >70) include corn flakes, baked potato, watermelon, croissant, white bread, extruded cereals (eg, Rice Krispies), straight glucose (100)

Question 65

A 32 year old lady with a 14 year history of type 1 diabetes is reviewed in clinic. She is currently managed with a basal bolus insulin regimen comprising of insulin glargine at a dose of 38 units at night coupled with variable preprandial doses of humalog. She has recently completed the DAFNE patient education program and her most recent Hba1c is 62.8 mmol/mol (7.9%) (<42.1 mmol/mol (6)). Her frequency of hypoglycaemia has significantly reduced since she completed the DAFNE course, but she is still experiencing some high blood sugar levels in the afternoon and early evening and requests further information on the glycaemic load of food in relation to her glycaemic control.

Which of the following is the most appropriate advice relating to glycaemic load for this lady?

- **A)** The glycaemic load is closely related to the glycaemic index of food
- **B)** The glycaemic load of a serving of food can be calculated by its carbohydrate content divided by its glycaemic index and multiplied by 100
- **C)** The glycaemic load of a serving of food can be calculated from its carbohydrate content, multiplied by its glycaemic index, and divided by 100
- **D)** The glycaemic index and glycaemic load of a serving of food have the same effect on postprandial glucose excursions
- **E)** The glycaemic load of food reflects of insulin sensitivity

Answer

Correct answer : The glycaemic load of a serving of food can be calculated from its carbohydrate content, multiplied by its glycaemic index, and divided by 100

The glycaemic load (GL) is a ranking system for carbohydrate content in food portions based on their glycaemic index (GI) and the portion size.

The usefulness of glycaemic load is based on the idea that a high glycaemic index food consumed in small quantities would give the same effect as larger quantities of a low glycaemic index food on blood sugar. For example, white rice has a somewhat high GI, so eating 50g of white rice at one sitting would give a particular glucose curve in the blood, while 25g would give the same curve but at half the height. Since the peak height is probably the most important parameter for diabetes control, multiplying the amount of carbohydrates in a food serving by the glycaemic index gives an idea of how much effect an actual portion of food has on blood sugar level.

Glycaemic load is generally a useful concept in programs targeting health maintenance. Studies have shown that sustained spikes in blood sugar and insulin levels may lead to increased diabetes risk. The Shanghai Women's Health Study concluded that women whose diets had the highest glycaemic index were 21 percent more likely to develop type 2 diabetes than women whose diets had the lowest glycaemic index. Similar findings were reported in the Black Women's Health Study. A diet program that manages the glycaemic load aims to avoid sustained blood sugar spikes, and can help avoid onset of type 2 diabetes. For people with diabetes, glycaemic load is a highly recommended tool for managing blood sugar.

Glycaemic load for a single serving of a food can be calculated as the quantity (in grams) of its carbohydrate content, multiplied by its GI, and divided by 100. For example, a 100g serving of watermelon with a GI of 72 and a carbohydrate content of 5g (it contains a lot of water) makes the calculation 5*0.72=3.6, so the GL is 3.6. A food with a GI of 100 and a carbohydrate content of 10g has a GL of 10 (10*1=10), while a food with 100g carbohydrate and a GI of just 10 also has a GL of 10 (100*0.1=10).

Glycaemic load does not reflect insulin sensitivity but since different foods contain different amounts of carbohydrate it is a more useful measure of the effect of an individual serving of food on postprandial glucose levels than the glycaemic index of food alone. Glycaemic load also has a scale. Low is 10 or less, Medium is 11-19 and 20 or greater is considered high.

Question 66

A 56 year old lady with a five year history of type 2 diabetes is reviewed in the clinic following conversion to insulin 6 months previously by her GP. Her current medication includes metformin 1 gram twice daily, gliclazide 80 mg twice daily, insulin glargine 38 units at night, simvastatin 20 mg at night and ramipril 5 mg at night. On her examination blood pressure is 150 / 85 mmHg, her BMI is 35 kg/m^2 and her body weight is 84 kg. She attended the EXPERT patient education programme 3 months previously at which time her body weight was 77.2 kg and her Hba1c at this time measured 65.0 mmol/mol (8.1%). Her 3 month average blood glucose level on review of her glucose monitor is 15.1 mmol/l.

		Normal Ranges
Haemoglobin	13.8 g/dl	(11 - 16)
RBC	4.17×10^{12}	(3.8 - 5.6)
MCV	84 fl	(80 - 98)
Mean Cell Haemoglobin Concentrate	29.5 pg	(27 - 34)
Hba1c	54.1 mmol/mol (7.1%)	(<42.1 mmol/mol (6))
Total Cholesterol	4.1 mmol/l	(<4)
TSH	4.5 mu/l	(0.32 - 5.5)
eGFR	67 ml/min/1.73 m^2	(90 - 110)

Which of the following is the most likely explanation for the discrepancy between this lady's self monitored blood glucose levels and her Hba1c?

- **A)** Faulty blood glucose monitoring equipment
- **B)** Incorrect self blood glucose monitoring technique
- **C)** The presence of a Haemoglobinopathy
- **D)** Unrecognised hypoglycaemia
- **E)** Vitamin B12 deficiency

Answer

Correct answer : Unrecognised hypoglycaemia

Based on this lady's self monitored average glucose measurement you would expect this lady's Hba1c to be approximately 10%. This lady is unlikely to have a haemoglobinopathy as her haematological parameters are normal, while vitamin B12 deficiency would not interfere with the Hba1c assay. Incorrect blood glucose monitoring technique or defective blood glucose monitoring could account for the observed discrepancy between this lady's blood glucose monitoring data and her Hba1c measurement. Over a 3 month period this lady has achieved a Hba1c reduction of 1%, which would be associated with an expected weight gain of 2.5 to 3.5 kg. This lady has gained nearly 7 kg suggesting that she may be eating in response to hypoglycaemia or to avoid hypoglycaemia.

Question 67

A 32 year old lady with a 21 year history of type 1 diabetes is reviewed in clinic. She is currently taking a basal bolus insulin regimen with an average total daily dose of 81 units. Her glycaemic control is poor with a most recent Hab1c of 76.0 mmol/mol (9.1%) (<42.1 mmol/mol (6)). She has been unable to obtain an Hba1c < 69.4 mmol/mol (8.5%) despite completing the DAFNE program and trying multiple different insulin regimens. She was unable to manage CSII therapy successfully and has evidence of bilateral background diabetic retinopathy and peripheral sensory neuropathy. She is therefore keen to pursue the possibility of islet cell transplantation.

Which of the following is the most appropriate information for this lady regarding islet cell transplantation?

- **A)** 50% of patients who receive islet cell transplantation will demonstrate insulin independence 2 years following their final islet cell infusion
- **B)** Around 10% of patients remain free of insulin injections five years after transplantation.
- **C)** Islet cell transplantation requires an open surgical procedure
- **D)** Long term post-transplantation corticosteroid based immunosuppressant therapy is required
- **E)** Nearly all patients who receive islet cell transplantation will achieve insulin independence at 1 year following transplantation

Answer

Correct answer : Around 10% of patients remain free of insulin injections five years after transplantation.

Experience to date with islet cell transplantation suggests that nearly two-thirds of recipients achieve “insulin independence”—defined as being able to stop insulin injections for at least 14 days—during the year following transplantation. Insulin independence is however difficult to maintain over time. Six months after their last infusion of islets, more than half of recipients are free of the need for insulin injections, but at 2-year follow-up, the proportion drops to about one-third of recipients. 5 years after transplantation only around 10% of patients demonstrate insulin independence. Other reported benefits of islet cell transplantation include improved blood glucose control, and greatly reduced risk of episodes of severe hypoglycaemia.
Transplants are often performed by a radiologist, using x rays and ultrasound to guide placement of a catheter through the upper abdomen and into the portal vein of the liver. The islets are then infused slowly through the catheter into the liver. Specialized enzymes are used to remove islets from the pancreas of a deceased donor. Because the islets are fragile, transplantation occurs soon after they are removed. Typically a patient receives at least 10,000 islet “equivalents” per kilogram of body weight, extracted from two donor pancreases. Patients often require two transplants to achieve insulin independence
Rejection is the biggest problem with any transplant, the use of immunosuppressive corticosteroid based immunosuppression may have a detrimental metabolic effect, due to increased insulin resistance. Currently the Edmonton protocol of immunosuppressive drugs is used, which includes daclizumab, sirolimus and tacrolimus.

Question 68

You see a 58 year old man with type 2 diabetes in the clinic. His HbA1c is 55.2 mmol/mol (7.2%) (<42.1 mmol/mol (6)) and he has had diabetes for 16 years. He has pre-proliferative retinopathy in his right eye and has had 1000 laser burns to treat this. He has not had any treatment to his left eye which shows severe background retinopathy. He has recently been diagnosed with angina and has been advised to take aspirin 150 mg once daily.
What advice would you give him?

- **A)** He should not take aspirin as this will lead to an increased risk of bleeding into his eyes.
- **B)** He should take clopidogrel not aspirin
- **C)** He should take aspirin with tranexamic acid to reduce the risk of bleeding into his eyes
- **D)** He should take aspirin as recommended as there is no increased risk of bleeding into his eyes.
- **E)** He should take aspirin as recommended as it will reduce the risk of his retinopathy progressing

Answer

Correct answer : He should take aspirin as recommended as there is no increased risk of bleeding into his eyes.

Aspirin is safe in severe non-proliferative diabetic retinopathy and does not appear to increase the risk of bleeding, nor however does it protect from retinopathy progression. There is no evidence to make a comment on whether clopidogrel is any different in its effect than aspirin. Equally there is no evidence to support using tranexamic acid.

Question 69

A 53 year old man with a 4 year history of type 2 diabetes who is currently self-employed as a taxi driver is reviewed in clinic. His current medication includes metformin 1 g od, sitagliptin 100mg od, simvastatin 20 mg od and enalapril 5 mg od. On examination, his blood pressure is 146/76 mmHg, his BMI is 33 kg/m^2, his visual acuity is 6/9 in the right eye and 6/6 in the left eye. His metabolic control is good with his most recent HbA1c being 51.9 mmol/mol (6.9%) (<42.1 mmol/mol (6)). His main concern relates to the effect diabetes may have on his eye sight and in particular how this may influence his ability to drive.

When assessing a patient's fitness to drive which of the following is most accurate?

- **A)** The best corrected visual acuity must be 6/12 or better in one eye
- **B)** The best corrected visual acuity should be 6/9 or better in both eyes
- **C)** The patient may not drive if there is a visual field defect in one eye
- **D)** Proliferative retinopathy is an automatic bar to driving
- **E)** The patient should be able to read a number plate at 25 meters

Answer

Correct answer : The best corrected visual acuity must be 6/12 or better in one eye

The best corrected acuity should be better than 6/12 in one eye only as long as the unaided acuity is not worse than 6/60 in the other eye. A visual field defect should be covered by the other eye to be able to drive but does not in itself stop driving, nor does proliferative retinopathy as long as the acuity is satisfactory. The patient needs to be able to read a number plate at 20 meters.

DVLA regulations relating to retinopathy and driving

Question 70

A 27 year old lady has developed gestational diabetes (GDM) during her first pregnancy. She has no family history of diabetes. She has required insulin therapy from 28 weeks gestation in the form of a basal bolus regimen with an insulin requirement of 70 units over 24 hours. Following an uneventful delivery, which of the following should she be advised to do?

- **A)** Continue with her present insulin
- **B)** Reduce the dose of daily insulin
- **C)** Stop insulin and commence metformin
- **D)** Stop Insulin and commence on a sulphonylurea
- **E)** Stop all treatment

Answer

Correct answer : Stop all treatment

Gestational diabetes generally resolves once the baby is born. Based on different studies, the chances of developing GDM in a second pregnancy are between 30 and 84%, depending on ethnic background and presence of other risk factors for diabetes such as obesity, metabolic syndrome and family history. This patient should be re-screened with a fasting plasma glucose measurement at the 6-week postnatal health check and annually thereafter, as she is at a high risk of developing subsequent diabetes since women who required insulin treatment or who have positive glutamate decarboxylase (GAD) or islet cell antibodies (ICA) are at higher risk of future diabetes.

Reference:

https://www.nice.org.uk/guidance/ng3

Question 71

A 24 year old Asian lady with a strong family history of type 2 diabetes undergoes an oral glucose tolerance test at 24 weeks gestation during her first pregnancy. The results of her 75 g oral glucose tolerance test are outlined below. She had already made changes to her diet and life style.Fasting and 2 hour self blood glucose monitoring over the subsequent 2 weeks reveal an average fasting glucose of 5.4 mmol/l and 2-hour value of 6.7 mmol/l.

		Normal Ranges
Fasting Blood Glucose Level	5.8 mmol/L	(5.3 mmol/l)
1 Hour Blood Glucose Level	10.1 mmol/l	(<10 mmol/L)
2 Hour Blood Glucose Level	9.3 mmol/l	(<8.6 mmol/L)
3 Hour Blood Glucose Level	8.2 mmol/l	(<7.8 mmol/L)

Which is the most appropriate initial management for this lady?

- **A)** Dietary / lifestyle modification
- **B)** Basal bolus insulin
- **C)** Metformin
- **D)** Once daily basal insulin
- **E)** Sulphonylurea

Answer

Correct answer : Metformin

We currently follow the NICE Guidelines for gestational diabetes 2015:

Diagnose gestational diabetes if the woman has either:

- a fasting plasma glucose level of 5.6 mmol/litre or above
- a 2-hour plasma glucose level of 7.8 mmol/litre or above.

Offer a trial of changes in diet and exercise to women with gestational diabetes who have a fasting plasma glucose level below 7 mmol/litre at diagnosis.

Offer metformin twice daily to women with gestational diabetes if blood glucose targets of fasting glucose of 5.3 mmol/L and 2 hour postprandial glucose level of 6.4 mmol/L are not met using changes in diet and exercise within 1–2 weeks.

Offer insulin instead of metformin to women with gestational diabetes if metformin is contraindicated or unacceptable to the woman. Offer addition of insulin to the treatments of changes in diet, exercise and metformin twice daily for women with gestational diabetes if blood glucose targets are not met.

Question 72

A 23 year old lady with a previous history of gestational diabetes during her first pregnancy 18 months previously undergoes a 75 gram oral glucose tolerance test at week 24 of her second pregnancy. This reveals a 2hr post OGTT glucose of 14.5 mmol/l. She is subsequently commenced on a basal bolus insulin regimen at an initial total daily dosage of 64 units. According to NICE guidelines, which of the following are appropriate capillary blood glucose targets for this lady?

- **A)** Fasting <5 mmol/l and 1 hour post-prandial < 7.1 mmol/l
- **B)** Fasting <5.3 mmol/l and 1 hour post-prandial < 7.8 mmol/l
- **C)** Fasting <5.9 mmol/l and 1 hour post-prandial < 8.1 mmol/l
- **D)** Fasting <6.1 mmol/l and 1 hour post-prandial < 8.5 mmol/l
- **E)** Fasting <6.9 mmol/l and 1 hour post-prandial < 8.5 mmol/l

Answer

Correct answer : Fasting <5.3 mmol/l and 1 hour post-prandial < 7.8 mmol/l

In accordance with NICE guidelines, blood glucose targets during pregnancy for women with diabetes (including gestational diabetes) care:

- A fasting value of less than 5.3 mmol/L
- A 1 hour postprandial value of less than 7.8 mmol/l

The recommendations for self-monitoring of blood glucose during pregnancy are to:

- Test fasting blood glucose levels
- Test blood glucose 1 hour after eating

Reference:
"https://www.nice.org.uk/guidance/ng3/chapter/1-Recommendations#antenatal-care-for-women-with-diabetes-2"

Question 73

A 32 year old Asian lady with a 2 year history of type 2 diabetes is referred by her GP following a positive pregnancy test subsequent to a two month period of amenorrhea. Her glycaemic control has been good, with a most recent HbA1c of 45.4 mmol/mol (6.3%) (<42.1 mmol/mol (6)). She is currently only taking metformin 500 mg twice daily and on examination her BMI is 33 kg /m^2 and her blood pressure is 132/70 mmHg.

Which of the following is the most appropriate initial approach for managing this lady's diabetes?

- **A)** Commence basal insulin
- **B)** Commence basal-bolus insulin
- **C)** Commence biphasic insulin
- **D)** Continue metformin
- **E)** Commence sulphonylurea

Answer

Correct answer : Continue metformin

A recent randomized controlled trial of metformin versus insulin showed that women preferred metformin tablets to insulin injections, and that metformin is safe and equally effective as insulin. Metformin in this case would also have additional potential benefits of a low risk of hypoglycaemia coupled with no detrimental weight effect.

Question 74

A 32 year old lady with a strong family history of type 2 diabetes is referred by her GP at 14 weeks gestation during her first pregnancy. She is concerned about the possibility of developing diabetes during her pregnancy. She undergoes a 75 gram oral glucose tolerance test the results of which are outlined below.

Fasting Plasma Glucose	5.3 mmol/l
1-hour post challenge plasma glucose	8.1 mmol/l
2-hour post challenge plasma glucose	7.7 mmol/l

Which of the following is the correct interpretation of these data?

- **A)** Gestational diabetes
- **B)** Impaired glucose tolerance
- **C)** Impaired fasting plasma glucose
- **D)** Normal glucose tolerance
- **E)** Combined impaired fasting glucose and impaired glucose tolerance

Answer

Correct answer : Normal glucose tolerance

Diagnose gestational diabetes if the woman has either:

a fasting plasma glucose level of 5.6 mmol/litre or above or

a 2-hour plasma glucose level of 7.8 mmol/litre or above.

Diabetes in pregnancy NICE guidelines (2015) NG3, gestational diabetes: risk assessment, testing, diagnosis and management

Question 75

A 21 year Asian lady has developed gestational diabetes during her first pregnancy. She has no family history of diabetes. She has required insulin therapy from 28 weeks gestation in the form of a basal bolus regimen with an insulin requirement of 68 units over 24 hours. 2 weeks subsequent to an uneventful delivery she no longer requires insulin and has a fasting plasma glucose of 5.5 mmol/l and random self-measured capillary glucose levels no greater than 7.9 mmol/l.

What is the risk of this lady progressing to develop diabetes over the next 5 years?

- **A)** < 1 %
- **B)** 5 - 10%
- **C)** 10 - 20%
- **D)** 25 - 35%
- **E)** > 80%

Answer

Correct answer : 25 - 35%

Women diagnosed with gestational diabetes have an increased risk of developing diabetes mellitus in the future. The risk is highest in women who needed insulin treatment, had antibodies associated with diabetes (such as antibodies against glutamate decarboxylase and islet cell antibodies), women with more than two previous pregnancies, and women who were obese and exhibiting features of the metabolic syndrome (in order of importance). Women requiring insulin to manage gestational diabetes have a 25-35% risk of developing diabetes within the next five years. Depending on the population studied, the diagnostic criteria and the length of follow-up, the risk can vary enormously. The risk appears to be highest in the first 5 years, reaching a plateau thereafter. In populations with a low risk for type 2 diabetes, in lean subjects and in patients with autoantibodies, there is a higher rate of women developing type 1 diabetes.

Further Reading:

Impact of gestational diabetes on the risk of diabetes following pregnancy among Chinese and South Asian women.

Question 76

A 35 year old lay with a 3 year history of type 2 diabetes is referred to ante-natal clinic at 14 weeks gestation. Her current medication includes metformin 500 mg three times a day only. On examination, her blood pressure is 136/74 mmHg, her BMI is 35 kg/m ^{2} and she has no clinical evidence of microvascular complications.

		Normal Ranges
HbA1c	58.5 mmol/mol (7.5%)	(<42.1 mmol/mol (6))
TSH	0.98 mu/l	(0.32 - 5.5)
U+E	Normal	
eGFR	96 ml/min/1.73m²	(90-110)

Which of the following would be the most appropriate method of managing this lady's glycaemic control?

- **A)** Increase metformin dose
- **B)** Add GLP1 analogue
- **C)** Add thiazolidinedione
- **D)** Commence basal-bolus insulin
- **E)** Commence twice daily biphasic insulin

Answer

Correct answer : Commence basal-bolus insulin

This lady has suboptimal glycaemic control on metformin monotherapy. An optimal level of glucose control should be defined by an HbA1c target < 47.5 mmol/mol (6.5%). This would be best achieved with conversion to a basal bolus insulin regimen. GLP1 and Thiazolidinediones are not recommended during pregnancy, while biphasic insulin would not represent the most effective means of managing both fasting and postprandial glucose levels. Analogue basal and prandial insulins may be safely used in such a regimen. Current evidence suggests that continuing with metformin in combination with insulin may be appropriate to reduce insulin requirements as there is no evidence of a detrimental effect of metformin on pregnancy outcome.

Question 77

A 24 year old lady attends clinic 6-8 weeks following the birth of her first baby. The delivery was uncomplicated, but during her pregnancy she developed gestational diabetes and was commenced on basal bolus insulin at 22 weeks requiring a total of 54 units daily. On examination, her blood pressure is 122/66 mmHg, her BMI is 29 kg/m^2 , her body weight is 65 kg and her waist circumference is 81 cm. She was found to be GAD antibody negative when she initially developed gestational diabetes and has no family history of diabetes. She is concerned about the possibility of developing diabetes in the future and since discontinuing insulin after her delivery she has been monitoring her blood glucose levels two to three times daily. On review of her meter, she has an average glucose level of 8.9 mmol/l. She returns to clinic the next morning and her fasting plasma glucose is taken and found to be 7.6 mmol/l.

What is the current diagnosis for this lady based on her self monitored glucose profile?

- **A)** Diabetes
- **B)** Impaired glucose tolerance
- **C)** Impaired fasting glucose
- **D)** Combined impaired glucose tolerance and impaired fasting glycaemia
- **E)** Normal glucose tolerance

Answer

Correct answer : Diabetes

Based on this lady's average glucose of 8.6 mmol/l she is likely to have a HbA1c of around 53 - 58.5 mmol/mol (7 – 7.5%) (52 -58mmol/mol) based on the A1c derived average glucose calculation (Av Glucose = 1.583 X A1c – 2.52). She is at high risk of subsequent diabetes following her pregnancy since she required around 0.8 u / kg of insulin, although she has no family history of diabetes and is GAD negative. Positive family history, GAD positivity and features of the metabolic syndrome further increase the risk of incidental diabetes following gestational diabetes. Based on this glucose profile alone it is unclear whether this lady has type 1 or type 2 diabetes.

Reference:

NICE clinical guidelines 63: Diabetes in pregnancy

Question 78

A 25 year old lady attends antenatal clinic at 14 weeks gestation, having recently been commenced on basal bolus insulin following a diagnosis of gestational diabetes. She has no family history of diabetes, but was diagnosed with gestational diabetes during her first pregnancy 2 years previously which resulted in the successful birth of a 5.3 kg baby boy. On examination her blood pressure is 135/75 mmHg, her BMI is 31 kg/m^2her waist circumference is 84 cm and fundoscopy reveals no evidence of retinopathy

What should be the HbA1c target for this lady during her pregnancy?

- **A)** < 36.6 mmol/mol (5.5%)
- **B)** < 43.2 mmol/mol (6.1%)
- **C)** < 47.5 mmol/mol (6.5%)
- **D)** < 53.0 mmol/mol (7%
- **E)** Do not measure Hba1c.

Answer

Correct answer : Do not measure Hba1c.

Current NICE guidelines do not recommend using HbA1c during pregnancy, as physiological changes mean that lower levels of HbA1c are obtained for equivalent blood glucose profiles. According to NICE guidelines diagnose gestational diabetes if the woman has either: a fasting plasma glucose level of 5.6 mmol/litre or above or a 2-hour plasma glucose level of 7.8 mmol/litre or above.

Question 79

A 26 year old nurse attends the diabetes clinic to discuss preconception advice. She has a 12 year history of type 1 diabetes with her most recent HbA1c being 65.0 mmol/mol (8.1%) (<42.1 mmol/mol (6)), her current medication includes humalog and insulin glargine via a basal bolus regimen amount to a total of 66 units per day.

On examination her blood pressure is 125 / 65 mmHg, her BMI is 25 kg / m^2, her body weight is 69 kg and she has no clinical evidence of microvascular complications.

What would be target HbA1c for this lady to safely achieve prior to conceiving (according to the NICE guidelines)?

- **A)** < 43.2 mmol/mol (6.1%)
- **B)** < 47.5 mmol/mol (6.5%)
- **C)** < 53.0 mmol/mol (7%)
- **D)** < 58.5 mmol/mol (7.5%)
- **E)** < 63.9 mmol/mol (8%)

Answer

Correct answer : < 47.5 mmol/mol (6.5%)

NICE guidelines recommend an optimal HbA1c below 47.5 mmol/mol (6.5%)if this can be safely achieved. An HbA1c below 53.0 (7%) is satisfactory, unless lower results could be safely obtained with more intensive therapy. NICE recommend that women with HbA1c above 85.8 mmol/mol (10%) avoid pregnancy.

Question 80

A 27 year lady with a 14 year history of type 1 diabetes attends the antenatal clinic at around 12 weeks gestation during her first pregnancy. Her current medication includes novorapid and insulin detemir at a total daily dose of 72 units via a basal bolus regimen.

On examination her blood pressure is 115 / 75 mmHg, her BMI is 28.5 kg/m^2 and her body weight is 77 kg. Her Hba1c is 57 mmol/mol (7.4%) (<42.1 mmol/mol (6)) and retinal screening carried out 6 months previously revealed the presence of background retinopathy in both eyes.

What frequency of retinal screening should be offered to this lady during her pregnancy?

- **A)** Screen once at 20 weeks gestation
- **B)** Screen once at 28 weeks gestation
- **C)** Screen at initial antenatal visit and again at 28 weeks
- **D)** Screen at initial antenatal visit and again at 16 - 20 weeks and then at 28 weeks
- **E)** Screen at 28 weeks and then at 12 weeks postpartum

Answer

Correct answer : Screen at initial antenatal visit and again at 16 - 20 weeks and then at 28 weeks

Progression of diabetic retinopathy may occur during pregnancy. The worsening of retinopathy during pregnancy can be quite significant and may require photocoagulation during pregnancy, more frequently in those patients with pre-existing diabetic retinopathy. The known risk factors for progression of diabetic retinopathy in pregnancy are summarized below:

1. Pregnancy is independently associated with progression of diabetic retinopathy
2. Baseline severity of retinopathy
3. Poor metabolic control at conception
4. Rapid improvement of glycaemic control
5. Poor metabolic control during pregnancy or the early postpartum period
6. Duration of diabetes
7. Chronic hypertension and pregnancy-induced hypertension

NICE guidelines recommend retinal assessment should be carried out by digital imaging with mydriasis using tropicamide. Recommendations from the National Screening Program are:

1. Annual Screening for diabetic retinopathy is recommended in the preconception period using two-field mydriatic digital photography using tropicamide.
2. Women with type 1 and type 2 diabetes should be offered two-field mydriatic digital photography to national standards at (or soon after) their first antenatal clinic visit and again at 28 weeks' gestation.
3. If background diabetic retinopathy is found to be present, an additional screen should be performed at 16-20 weeks.
4. If referable diabetic retinopathy is found to be present in early pregnancy, careful ophthalmological supervision is required depending on the level of retinopathy both during pregnancy and for at least 6 months postpartum.
5. Because, like many drugs that are used in pregnancy, tropicamide is only licensed for use in pregnancy under the direction of a registered medical practitioner, care pathways should be set up in such a way as to enable this to be undertaken.

Question 81

A 56 year old man with a 4 year history of type 2 diabetes attends clinic for routine review. His current medication includes metformin 500 mg three times daily, gliclazide 80 mg twice daily, simvastatin 20 mg once daily and lisinopril 10 mg once daily. On examination, his blood pressure is 146/76 mmHg, his BMI is 32 kg / m^2 and visual acuity is 6 / 9 in both eyes.

		Normal Ranges
HbA1c	60.7 mmol/mol (7.7%)	(<42.1 mmol/mol (6))
Total Cholesterol	4.2 mmol/l	(<4)
Plasma Triglyceride	1.9 mmol/l	(0.9 - 2.2
eGFR	76 ml/min 1.73 m^2	(90-110)
Urine Albumin to Creatinine Ratio (ACR)	1.9 mg/mmol	(<2.5)

When eGFR >60 ml/min/1.73m^2 , what increase in Serum Cr denotes significant renal function reduction ?

- **A)** 5%
- **B)** 10%
- **C)** 20%
- **D)** 50%
- **E)** Changes in serum creatinine are not accurate

Answer

Correct answer : 20%

An increase in serum creatinine > 20%, when eGFR > 60 ml/min/1.73 m^2 suggests a significant deterioration in renal function, indicating the need for further investigation. However a rise in serum creatinine of up to 20% on initiation of ACE-I or ARB therapy is considered to represent a normal physiological response, a greater increase may be indicative of renovascular disease.

Question 82

A 49-year-old lady with a 32-year history of type 1 diabetes on review in the clinic complains of a persistent burning sensation in both feet which has been an ongoing problem for the last 2 years and has shown no symptomatic response to co-dydramol and non-steroidal based analgesia. She has had chronic sub-optimal glucose control with a most recent Hba1c measuring 73.8 mmol/mol (8.9%) (<42.1 mmol/mol (6)).

On examination her blood pressure is 145/75 mmHg, her BMI is 29 kg/m^2 examination of her feet reveals preserved dorsalis pedis pulses and posterior tibial pulses with reduced vibration and proprioception sensation along with a biothesiometer reading of 20V.

Which of the following would be the most appropriate therapeutic option for managing this lady's symptoms?

- **A)** Carbamazepine 100 mg daily
- **B)** Duloxetine 60 mg daily
- **C)** Fluoxetine 20 mg daily
- **D)** Gabapentin 900 mg daily
- **E)** Improve glycaemic control

Answer

Correct answer : Duloxetine 60 mg daily

In accordance with NICE guidelines 173, for people with painful diabetic neuropathy, offer oral duloxetine 60 mg, amitriptyline, pregabalin or gabapentin. If satisfactory pain reduction is still not achieved with maximisation then switch to another 1st line agent. In this case duloxetine is the right answer as the dose for gabapentin is too high for initiation.

Tight control of blood glucose can reverse the changes of diabetic neuropathy, but only if the neuropathy and diabetes is recent in onset. Conversely, painful symptoms of neuropathy in uncontrolled diabetics tend to subside as the disease and numbness progress. Of course, these uncontrolled patients are at great risk for diabetic foot ulcers and amputation.

Reference:

NICE clinical guidelines 173: Neuropathic pain

Further reading: Diabetic Neuroptahy

Question 83

A 65 year old gentleman with a 6 year history of type 2 diabetes is reviewed in clinic and complains of a dead feeling in his left foot that over the last few weeks has become increasingly painful with episodes of stabbing pain and electric shock-like symptoms, which do not appear to be related to exercise. He also complains of lower back pain. His current medication includes metformin 500 mg three times daily, gliclazide 160 mg twice daily, sitagliptin 100mg od, simvastatin 20 mg once daily and lisinopril 20 mg once daily.

On examination his blood pressure is 145/85 mmHg and his BMI is 35 kg/m^2. Lower limb neurological examination reveals reduced vibration, proprioception, thermosensation and 10 g microfilament sensation in the left foot along with an absent left ankle jerk. Sensory modalities appear preserved as are all reflexes in the right foot. There is no evidence of muscle wasting and both dorsalis pedis and posterior tibial pulses are palpable bilaterally.

Investigations reveal:

		Normal Ranges
HbA1c	67.2 mmol/mol (8.3%)	(<42.1 mmol/mol (6))
Total Cholesterol	4.7 mmol/l	(<4)
Plasma TG	1.9 mmol/l	(0.9 - 2.2)
eGFR	78 ml/min/1.73 m^2	
Urine Albumin:Creatinine Ratio	1.8 mg/mmol creat	(<2.5)

What is the most likely cause of this man's symptoms?

- **A)** Diabetic peripheral neuropathy
- **B)** Cauda equina syndrome
- **C)** Mononeuritis multiplex
- **D)** Peripheral vascular disease
- **E)** Prolapsed intervertebral disc

Answer

Correct answer : Prolapsed intervertebral disc

Mononeuritis multiplex involves damage to at least 2 separate nerve areas. This condition can become progressively worse over time. The damage to the nerves involves destruction of the axon, thus interfering with nerve conduction. Common causes of damage include a lack of oxygen from decreased blood flow or inflammation of blood vessels. Pain is usually an initial presenting feature of mononeuritis multiplex, which is usually described as deep and aching with superimposed lancinating jabs. Loss of sensation and movement may be associated with dysfunction of specific nerves.

Cauda equina syndrome results from acute loss of function of the neurologic elements (nerve roots) of the spinal canal below the termination (conus) of the spinal cord, with signs arising due to loss of function related to the injured nerves.

Diabetic peripheral neuropathy usually produces bilateral signs and symptoms and the fact that peripheral pulses are present and that the symptoms are not in keeping with claudication make a diagnosis of peripheral vascular disease also unlikely in this case.

A prolapsed intervertebral disc resulting in lumbosacral nerve root compression would produce symptoms and signs such as those demonstrated by this gentleman and further investigation with a lumbosacral MRI would be appropriate.

Question 84

A 77 year old man with a 24 year history of type 2 diabetes is reviewed in clinic he feels tired but denies any osmotic symptoms. His current therapy includes ‘novomix 30’ 32 units in the morning and 24 units in the evening, ramipril 5 mg daily, simvastatin 40 mg daily, indapamide 1.5 mg daily and aspirin 75 mg daily. On examination his blood pressure is 134 /66 mmHg, his body weight is stable at 86 kg, his BMI is 32 kg / m^2 and he has reduced vibration and proprioception sensation in both feet.
Investigations reveal:

		Normal Ranges
Hab1c	60.7 mmol/mol (7.7%)	(<42.1 mmol/mol (6))
Total Cholesterol	4.4 mmol/l	(<5)
Haemoglobin	10.1 g/dl	(12-16)
MCV	86 pl	(76-98)
Ferritin	88 mmol/l	(15 - 300)
eGFR	38 ml/min/1.73 m²	(90 - 110)
Urine Albumin to Creatinine Ratio (ACR)	7.9 mg/mmol creat	(<2.5)

Which of the following is the most appropriate approach for the management of this gentleman’s anaemia?

- **A)** EPO should not be considered until his eGFR is < 30 ml/min/1.73 m^2
- **B)** EPO would be contra-indicated due to sub-optimal blood pressure control
- **C)** He should receive iron supplementation only
- **D)** He should receive iron supplementation prior to considering therapy with EPO
- **E)** He does not require any treatment for his anaemia at current levels

Answer

Correct answer : He should receive iron supplementation prior to considering therapy with EPO

The failure of erythropoietin production and subsequent development of anaemia is more common in patients with diabetes, particularly females with type 1 diabetes. Co-existent autonomic neuropathy may be an important factor as release of erythropoietin is modulated by the sympathetic nervous system. Urinary erythropoietin losses, interstitial fibrosis (90% of erythropoietin is produced by peritubular fibroblasts) and angiotensin converting enzyme inhibition may also be factors.

Patients with anaemia secondary to diabetic kidney disease, however demonstrate no difference in response to exogenous erythropoietin compared with patients with non-diabetic kidney disease. Exogenous erythropoietin has been shown to reduce Hba1c levels, thus when evaluating glycaemic control in patients undergoing therapy for renal anemia, Hba1c estimation alone may be insufficient. It has long been postulated that correction of renal anaemia will have a positive effect on mortality. This seems likely but at what level of haemoglobin (Hb) this benefit would become evident is less clear.

Raising haematocrit by 25% has been shown to reduce left ventricular mass and cross sectional analyses have demonstrated increased mortality in patients with Hb < 11 g / dl compared to those with Hb levels > 11 g /dl. Patients treated to a Hb level > 13.5 g / dl have been shown to experience higher incidence of congestive heart failure, stroke, myocardial infarction and death. Consequently, current guidelines advocate that treatment should maintain stable Hb concentrations between 10.5 and 12.5 g / dl, with adjustments to treatment considered when Hb levels < 11.0 g / dl or >12.0 g / dl. Age alone should not be a determinant of treatment for renal anaemia. Appropriate iron stores are required for the optimal management of renal anaemia with EPO and this is defined by a serum ferritin concentration of between 200 and 500 µg / l combined with either a transferrin saturation > 20% (unless ferritin > 800 µg / l) or percentage hypochromic red cells < 6%(unless ferritin > 800 µg / l).

Question 85

A 46 year old man of Afro-Caribbean origin has recently been diagnosed type 2 diabetes managed by lifestyle modification. He has no previous medical history of note. On examination his blood pressure is 155 / 80 mmHg, his body weight is 94 Kg, his BMI is 34 kg/m^2 and direct fundoscopy is normal.
Investigations reveal:

		Normal Ranges
Hba1c	51.9 mmol/mol (6.9%)	(<42.1 mmol/mol (6))
Total Cholesterol	4.9 mmol/l	(<4)
eGFR	58 ml/min/1.73m²	(90 - 110)
Serum Creatinine	128 µmol/l	(56 - 102)
Urine Albumin Creatinine Ratio	1.9 mg.mmol/creat	(<2.5)

Which of the following is the most appropriate approach to the evaluation of this gentleman's renal function?

- **A)** His renal function can be assessed by monitoring his serum creatinine since serum creatinine bears a linear relationship with glomerular function
- **B)** eGFR measurements would not be an accurate means of following his renal function as eGFR underestimates true GFR in people with diabetes with GFR values GFR < 60 ml/min/ 1.73m^2
- **C)** eGFR calculations for this gentleman require correction by multiplying by a factor of 1.2.
- **D)** This gentleman has chronic kidney disease (CKD) stage 3 and should be treated to a blood pressure target of 130 / 80
- **E)** Blood pressure is the primary determinant of this gentleman's kidney function

Answer

Correct answer : eGFR calculations for this gentleman require correction by multiplying by a factor of 1.2.

Glomerular filtration rate (GFR) is the gold standard measure of renal function and has a non-linear relationship with serum creatinine. There are three physiological determinants of GFR namely, ultrafiltration pressure, permeability of the glomerular wall and surface area of capillary available for filtration. GFR is important because as it reduces, for reasons not completely clear, there is an associated increase risk of cardiovascular disease. In the South Tees Mortality study the adjusted hazard ratio for ischaemic heart disease was 3.6 and 8.1 fold higher for those with eGFR 30 – 59 and < 30 ml/ min/1.73 m^2 respectively. Consequently, all patients with an eGFR < 60 ml/min/1.73 m^2 are defined as having chronic kidney disease irrespective of their urinalysis. The MDRD equation is used to calculate eGFR and this underestimates GFR particularly in patients with values > 60 ml/min /1.73 m^2. GFR varies according to gender, muscle mass and other factors such as physical exertion. MDRD derived eGFR values require correction by multiplying by 0.742 if female and by 1.212 if Afro-Caribbean.

This gentleman does not have CKD stage 3 as his corrected eGFR is 69 (58 X 1.2). Clinical determinants of renal function in people with diabetes include numerous factors including both blood pressure and blood glucose control.

Question 86

A 32 year old woman comes to clinic. She has been using continuous subcutaneous insulin infusion therapy for 3 years. Over the last 18 months her HbA1c has been < 58.5 mmol/mol (7.5%). She has lost 2 stone in weight and her BMI is now 23 kg/m^2. She has the following basal rates of insulin:

Midnight-6am	0.5 units/hour
6am-1pm	0.8 units/hour
1pm-6pm	0.7 units/hour
6pm-mitnight	0.9 units/hour

Her insulin to carbohydrate ratios are 1 unit to 10g at breakfast and lunch, 1unit to 15g at evening meal.
She has recently developed recurrent hypoglycemia 1 – 2 hours after lunch and finds this very difficult as she works as a secondary school teacher. How would you advise her?

- **A)** Lower all basal rates by 0.1units/hour
- **B)** Lower her basal rates by 0.1units/hour 1pm to 6pm
- **C)** Lower her basal rates by 0.1units / hour 6am - 1pm
- **D)** Alter her lunchtime insulin to carbohydrate ratio to 1 unit to 15g
- **E)** Increase the "low glycemic index" carbohydrate content of her lunch

Answer

Correct answer : Alter her lunchtime insulin to carbohydrate ratio to 1 unit to 15g

Meal time insulin requirements (bolus rates) are assessed by measuring glucose levels 2 hours post-prandially to ensure limited glucose excursion. She has lost 2 stone in weight and has therefore probably increased insulin sensitivity and needs less insulin for food at lunchtime. The other mealtime insulin requirements should also be assessed by measuring post-prandial glucose levels. If the basal rates are reduced, this may result in glucose levels being too high at other times of the day. Many modern pumps can give boluses of insulin over a protracted period of time e.g. over 1 hour to accommodate lower glycemic index meals. Apart from Reducing insulin dose, it is important to evaluate for the cause of weight loss, with Addison's being an important diagnosis to be excluded.

Question 87

A 23 year old woman has been on continuous subcutaneous insulin infusion for 1 year commenced 3 months into a pregnancy. Her control throughout pregnancy was acceptable with an HbA1c between 44.3 mmol/mol- 48.6 mmol/mol (6.2 to 6.6%). She is now 6 months postpartum. Her latest HbA1c is 80.3 mmol/mol (9.5%). She attends with a 2 day history of polyuria, abdominal pain and vomiting. She has given herself repeated boluses of insulin via the pump but her glucose levels remain >28 mmol/l. She is admitted to hospital with diabetic ketoacidosis and treated according to local policy. Once she has recovered which of the following is the appropriate course of action?

- **A)** Cessation of continuous subcutaneous insulin infusion therapy is indicated as she has had an episode of diabetic ketoacidosis
- **B)** Her insulin via the pump needs to be increased by 20%
- **C)** She should return to a basal bolus regime for 3 months to allow her insulin requirements to be recalculated.
- **D)** She should be advised to temporarily override to 150% of her usual basal rates if the situation recurs.
- **E)** She should be advised that if an initial bolus via the pump for hyperglycaemia does not lower her glucose then a bolus should be given by an insulin pen and the pump removed and the set-up procedure repeated.

Answer

Correct answer : She should be advised that if an initial bolus via the pump for hyperglycaemia does not lower her glucose then a bolus should be given by an insulin pen and the pump removed and the set-up procedure repeated.

Insulin delivery may become discontinued if there is a mechanical fault with the pump or if a cannula has become blocked or kinked and this can result in diabetic ketoacidosis. This can be prevented if the patient is educated to give an insulin bolus by pen or syringe if hyperglycaemia is not responding to boluses from the pump. This patient may have forgotten this rule particularly if the pump was commenced in an urgent manner when she had poor control or problems in pregnancy.

Question 88

A 53 year old on continuous subcutaneous insulin therapy is due to be admitted for a hysteroscopy and endometrial biopsy under general anaesthetic. She has been on continuous subcutaneous insulin infusion therapy for 5 years and has an HbA1c of 36.6 mmol/mol (5.5%) The anaesthetist contacts you for advice on glycaemic management during surgery. What will you advise?

- **A)** Stop the pump at midnight before the procedure and commence intravenous insulin and glucose at 6 am to cover the intra-operative procedure and restart the pump when eating and drinking.
- **B)** Continue the pump therapy with the anaesthetist monitoring the blood glucoses intra-operatively and giving intravenous glucose if needed.
- **C)** Switch to intravenous glucose and insulin the night before the procedure and continue until eating and drinking
- **D)** Discontinue the pump on induction of anaesthesia and observe glucoses. Start intravenous insulin if needed.
- **E)** Anaesthetist to alter the pump during the procedure and post-operatively.

Answer

Correct answer : Continue the pump therapy with the anaesthetist monitoring the blood glucoses intra-operatively and giving intravenous glucose if needed.

Hysteroscopy is a procedure requiring a short anaesthetic with an expected rapid recovery usually performed as a day case. If continuous subcutaneous insulin infusion therapy is stopped alternative insulin therapy should be started within 1 hour, ideally immediately. If the cessation is protracted hyperglycaemia is inevitable and diabetic ketoacidosis could result. Although using intravenous glucose and insulin therapy from the night before is not wrong, it is unlikely to be necessary and will result in an unnecessary hospital admission and hourly glucose estimations overnight which is disruptive. The anaesthetist is unlikely to be familiar enough with the pump mechanism to alter this and could monitor the glucoses and ensure hypoglycaemia does not occur during anaesthesia when it will not be detected.

Question 89

A 19 year old woman on continuous subcutaneous insulin infusion for 6 months comes to clinic. Her HbA1c is 8% (64mmol/mol). She is due to go to Australia for 2 months and has not previously travelled internationally with her pump. She asks for advice on monitoring her pump on the journey to Australia. How will you advise her?

- **A)** Continue with the usual basal rates as per UK time and temporarily override as needed.
- **B)** Set the pump at the lowest basal rate for the duration of the flight , bolus for food as usual and set the clock on the pump to local time on arrival
- **C)** Switch back to a basal bolus regime using insulin glargine and insulin aspart for the journey
- **D)** Set the basal rate to 0.2unit / hour and check blood glucoses every 2 hours and give insulin boluses as necessary
- **E)** Set the pump to 50% of usual basal rates and give insulin boluses as needed.

Answer

Correct answer : Set the pump at the lowest basal rate for the duration of the flight , bolus for food as usual and set the clock on the pump to local time on arrival

The usual basal rates alter depending on the time of day, the diurnal hormonal variations and usual routine and travel across several time zones will disrupt these factors. Setting the pump to the lowest usual basal rate allows travel to be safely undertaken and food boluses and correction boluses can be given as needed. If the pump clock is switched to local time on arrival the usual basal daily rates can resume with minimal disruption.

Question 90

A 28 year old man with type 1 diabetes mellitus is on continuous subcutaneous insulin infusion and presents for urgent review as he has developed problems with erratic glucose levels. He trains regularly in the gym and plays squash three times a week. He has found his glucoses need to be greater than 8 mmol/l prior to training or squash to prevent hypoglycaemia but that post training they are usually greater than 18 mmol/l. He eats a high carbohydrate meal with a usual bolus plus a correction bolus of 8 units of insulin after training but finds that overnight he is having hypoglycaemic episodes. How would you advise him?

- **A)** Give a bolus of insulin at the start of his squash match or training and reduce the basal rate throughout
- **B)** Give a bigger bolus of insulin with his post squash meal and increase basal rates to bedtime
- **C)** Increase the basal rates during the squash match / training
- **D)** Give a smaller bolus e.g. 4 units and keep the basal rates the same across the evening and night.
- **E)** Increase the basal rates leading up to the squash match / training

Answer

Correct answer : Give a bolus of insulin at the start of his squash match or training and reduce the basal rate throughout

Giving more insulin as a bolus or by increasing the basal rates before exercise may cause hypoglycaemia during exercise. The catecholamines released during exercise may cause hyperglycaemia and the extent may vary depending on the activity. Hypoglycaemia up to 24 hours after activity may occur. His bolus of 8 units of insulin is probably excessive for him and injecting the insulin just prior to exercise may help to reduce his post exercise hyperglycaemia; generally 1 unit of insulin will reduce the glucose by 2.5 mmol/l although this will vary depending on insulin sensitivity. Reducing his basal rates post exercise should help to prevent hypoglycaemia.

Question 91

A 30 year old man takes insulin lispro 6 units three times a day and insulin glargine 16 units. Despite efforts from the patient and diabetes team, his HbA1c remains greater than 74.9 mmol/mol (9%). Any increase in his insulin causes recurrent severe hypoglycaemia. He is to commence continuous subcutaneous insulin infusion. His starting basal rates should be:

- **A)** 0.5 units / hour
- **B)** 1.0 units / hour
- **C)** 1.5 units / hour
- **D)** 0.1 units / hour
- **E)** 0.8 units / hour

Answer

Correct answer : 0.5 units / hour

The initial basal rate is calculated by

1. Calculating total daily dose (TDD)insulin
2. Subtracting 25% to 30 % of TDD of Insulin
3. This dose is then halved
4. This result divided into 24 hours to give the starting basal rate.

Now calculate the basal rate:

- Short acting insulin = 18 units
- Long acting insulin = 16 units
- Total = 34 units
- -30% = approximately 24 units
- Divide by 2 = 12 units
- Divide by 24 hours = 12units/24 hours = 0.5 units/hour

Question 92

A child of 5 years of age has been on a continuous subcutaneous insulin infusion for 18 months. He is starting primary school and his mother is returning to work. His parents usually manage his pump and calculate and give his bolus doses. They have discussed his pump at length with his school staff who are comfortable with recognising and treating any hypoglycaemic episodes and also agree to unclip the pump for sports and re-attach the pump once the activity is concluded. The remaining issue is giving a bolus to cover his lunch as the school staff are unhappy to accept this responsibility. What would you advise?

- **A)** Arrange for a district nurse to visit the school to inject the child using a needle and syringe prior to lunch.
- **B)** Continue without a lunchtime bolus and encourage low glycaemic index food for this meal
- **C)** Continue without a bolus until the child is able to administer his own bolus which will probably be within 1 to 2 years
- **D)** Increase the basal rate for an hour over the period following lunch
- **E)** Switch to a different insulin regime such as a twice daily pre-mixed regimen until the child is able to manage his own pump

Answer

Correct answer : Increase the basal rate for an hour over the period following lunch

This can be a difficult issue when children have good glycaemic control but need to move to a situation where this may be compromised. Many children are competent to manage their pump by the age of 6 to 7. Switching to a pre-mixed insulin regimen would usually worsen the glycaemic control and be too restrictive to be acceptable. Leaving the child without a bolus is possible but will probably lead to hyperglycaemia and may cause polyuria and other symptoms of hyperglycaemia in the afternoon. A district nurse visiting to give an injection of insulin would not be wrong but would be restrictive and the injection is likely to be unwelcome. Increasing the basal rate is a compromise as it will not account accurately for the amount of food eaten and may cause a problem if the child refuses to eat when the only option for the school may be to unclip the pump for an hour.

Question 93

A 55 year old male presents with a two day history of pain in the left leg and fever. He has had type 2 diabetes diagnosed for three years and is treated with metformin 1g bd. On examination, he has a temperature of 37.5°C and has an erythematous swelling of the skin of the foot to the mid shin. It is noted that he has a small abrasion between the great toe and 2nd toe.

Which of the following is the most likely infective organism in this case?

- **A)** E. coli
- **B)** H. influenzae
- **C)** Methicillin resistant staphylococcus aureus
- **D)** Pseudomonas aeruginosa
- **E)** Streptococcus pyogenes

Answer

Correct answer : Streptococcus pyogenes

The patient has a classical description of cellulitis which is most likely to be due to either staphylococcus aureus (not typically MRSA) or streptococcus.

Question 94

A 45-year-old male of Afro-Caribbean origin presents with a 5-day history of feeling unwell with polyuria and nocturia. He had a past history of hypertension for which he was being treated with losartan and atorvastatin. He was also taking pantoprazole for reflux.

On examination, the clinician felt he could smell ketones. He had a BMI of 32kg/m^2, had a pulse of 100 bpm reg, seemed dehydrated and had a blood pressure of 108/76 mmHg with a respiratory rate of 22/min.

Investigations of relevance revealed:

Test	Result	Normal Range
Urea	12.3 mmol/l	(3-8)
Creatinine	160 micromol/l	(50-100)
Glucose	19.9 mmol/l	(3.5-5.5)
HbA1c	10.9% or 96 mmol/mol	
pH	7.27	
Blood ketones	4.1 mmol/l	(<0.6)

Besides IV fluids, which of the following is the most appropriate approach to the management of this patient at this stage?

- **A)** Treat with an oral sulphonylurea
- **B)** Treat with basal-bolus insulin regime
- **C)** Treat with fixed-rate insulin regime
- **D)** Treat with oral metformin
- **E)** Treat with variable rate insulin regime

Answer

Correct answer : Treat with fixed-rate insulin regime

Explanation:

This patient has diabetic ketoacidosis as revealed by an elevated glucose, low pH and elevated ketones. The most appropriate approach to the management of this patient is an IV fixed-rate insulin regime. This has been demonstrated to be superior to variable rate or sliding scale insulin infusion.

IV resuscitation with normal saline is also important in this case based on the associated acute kidney injury and again should follow a protocol as detailed in the following link from NICE.

Reference:

- NICE: Diabetic ketoacidosis

Question 95

A 52 year man presents with a 3 month history of general lethargy and polyuria over the last month, but he denies any obvious weight loss. He has no past medical history or family history of note.

On examination his body weight is 83 kg, his BMI is 30 kg /m^2 and his blood pressure measures 144/77 mmHg.

Investigations reveal:

		Normal Ranges
Fasting glucose	14.9 mmol/l	3.5-6
HbA1c	67.2 mmol/mol (8.3%)	< 42.1 mmol/mol (6%)
U+Es	Normal	

Urine analysis - Glucose +++ Ketones +

Which of the following is the most appropriate treatment for this man?

- **A)** Gliclazide
- **B)** Metformin
- **C)** Pioglitazone
- **D)** Once daily basal insulin
- **E)** Twice daily biphasic insulin

Answer

Correct answer : Metformin

The current NICE guideline update on blood glucose control (NG 28, JULY 2016) advocates metformin as the first line oral therapy in people with type 2 diabetes with sub-optimal glucose control (Hba1c ≥ 47.5 mmol/mol (6.5%)) unless the person is not overweight, metformin is contraindicated or not tolerated or the person requires rapid therapeutic response due to hyperglycaemic symptoms. This gentleman describes classic hyperglycaemic symptoms and the absence of any weight loss suggests that this patient does not currently require exogenous insulin.

Question 96

A 65 year old gentleman with a 3 year history of type 2 diabetes is reviewed in clinic. He feels generally well and has a fairly predictable lifestyle having been retired for the last 2 years. His current medication includes metformin 1 gram bd, ramipril 5 mg od and simvastatin 20 mg od. On examination there is no evidence of any microvascular complications, his blood pressure measures 145/75 mmHg, his body weight is 88 kg and his BMI is 31 kg/m^2.

		Normal Ranges
U+E	Normal	
HbA1c	52 mmol/mol (7.0%)	< 42.1 mmol/mol (6)
eGFR	79 mls/min/1.73m^2	>90
Total cholesterol	4.5 mmol/l	<5
LDL cholesterol	2.9 mmol/l	<3
HDL cholesterol	0.9 mmol/l	0.9-2
Triglyceride	1.9 mmol/l	0.9-2.1

Which of the following is the most appropriate management for this patient?

- **A)** Add exenatide
- **B)** Add empagliflozin
- **C)** Add gliclazide
- **D)** Add sitagliptin
- **E)** Continue with metformin alone

Answer

Correct answer : Continue with metformin alone

The current NICE guideline update on blood glucose control (NG 28) advocates the use of a 2nd line oral hypoglycaemic agent in people with type 2 diabetes with sub-optimal control (Hba1c ≥ 58 mmol/mol (7.5%)) receiving maximum tolerated metformin monotherapy. A TZD/ DPP-4i/SU or SGLT2 inhibitor are recommended. In this case, with the Hba1c at 54 mmol/mol the guidance does not suggest any requirement to optimise treatment.

Question 97

A 52 year old bus driver is reviewed in clinic. He has an 8 year history of type 2 diabetes and has background retinopathy affecting both eyes. He is generally well and denies any osmotic symptoms or weight loss. His current medication includes metformin 1 gram twice daily, gliclazide 160 mg twice daily, simvastatin 40 mg once daily and perindopril 4 mg once daily. On examination his body weight is 91 kg, his BMI is 31 kg/m^2 and his blood pressure measures 148/78 mmHg.
Investigations reveal:

		Normal Ranges
U+Es	Normal	
HbA1c	71.6 mmol/mol (8.7%)	< 42.1 mmol/mol (6)
eGFR	64 ml/min/1.73m^2	>90
Total cholesterol	4.1 mmol/l	<5
LDL cholesterol	2.2 mmol/l	<3
HDL cholesterol	0.8 mmol/l	0.9-2
Triglycerides	2.1 mmol/l	1.1-2.

He is not keen on SGLT2 inhibitors due to possible side effects. Which of the following would be the most appropriate therapeutic option for managing this man's glycaemic control?

- **A)** Add GLP-1 receptor agonist
- **B)** Add once daily NPH insulin
- **C)** Add once daily insulin glargine
- **D)** Add twice daily biphasic insulin
- **E)** Add meal time humalog

Answer

Correct answer : Add GLP-1 receptor agonist

The current NICE guideline update on blood glucose control suggests that in people failing to maintain adequate blood glucose control (Hba1c 58.5 mmol/mol (7.5%)) despite maximal oral therapy, insulin should be initiated in the form of either once or twice daily NPH insulin according to need, in the context of appropriate structured education. A basal insulin analogue is recommended if the person cannot use the device to deliver NPH insulin, optimal dose titration of NPH insulin is limited by hypoglycaemia, or the person needs help with injecting insulin and a once daily analogue insulin would replace twice daily NPH. GLP-1 analogues are currently recommended according to the NICE guidance as an alternative to exogenous insulin where insulin use would have detrimental effects on employment, or in people with a BMI of 35 kg /m^2 of European descent of where further weight gain would exacerbate problems associated with high body weight or in people with BMI 35 Kg /m^2 where insulin is unacceptable due to occupational implications or where weight reduction would benefit other co-morbidities. Biphasic insulin within the current NICE guidance may be considered as an option in people who are markedly hyperglycaemic e.g. Hba1c > 80.3 mmol/mol (9.5%).

Question 98

A 69 year old lady is reviewed in clinic. She has a six month history of type 2 diabetes which has been initially managed with lifestyle modification. She also has a five year history of treated hypertension. Her current medication includes amlodipine 5 mg once daily, simvastatin 20 mg once daily and aspirin 75 mg once daily.

On examination her body weight is 71 kg, her BMI is 29 kg/m^2 and her blood pressure is 155/75 mmHg. Investigations reveal:

		Normal Ranges
HbA1c	54.1 mmol/mol (7.1%)	< 42.1 mmol/mol (6)
eGFR	49 mls/min/1.73m2	90-110
Creatinine	128 micromol/l	50-100
Albumin/creatinine ratio	4.1 mg/mmol	<3.5
Fasting plasma glucose	6.1 mmol/l	3.5-6

Which of the following would be the most appropriate approach for managing this lady's blood glucose?

- **A)** Glibenclamide
- **B)** Gliclazide
- **C)** Metformin
- **D)** Pioglitazone
- **E)** Persist with current lifestyle changes alone

Answer

Correct answer : Metformin

The current NICE guideline update on blood glucose control (NG 28, JULY 2016) advocates the use of metformin as a first line oral hypoglycaemic agent in people with suboptimal glycaemic control (HbA1c ≥ 47.5 mmol/mol (6.5%)) unless it is contraindicated or not tolerated. In such situations a sulphonylurea of lowest acquisition cost – but not glibenclamide – is recommended. Sitagliptin, saxagliptin and alogliptin can be used with appropriate dose adjustments in relation to eGFR. Linagliptin 5mg OD can be used in renal impairment without any dose reductions.

Question 99

A 44 year old male is referred by his GP as he is concerned regarding a fasting plasma glucose value of 5.9 mmol/l and wonders what needs to be done about this. The patient informs you that he went to the GP as he was concerned about developing diabetes and he tells you that he has been thirsty on occasions and may get up in the night twice to urinate. He has a strong family history of diabetes with his mother and maternal uncle suffering from the disorder. He takes no medication

On examination, he has a BMI of 32.2 kg/m^2, blood pressure of 132/78 mmHg and he has central adiposity. A repeat fasting plasma glucose returns as 6.1 mmol/l (3.5-6).
You give the patient advice concerning the importance of diet and exercise with emphasis placed on weight loss. Which of the following would you suggest regarding further investigation of his glucose concentration?

- **A)** Arrange oral glucose tolerance test
- **B)** Check HbA1c
- **C)** Check fructosamine
- **D)** No further investigation required
- **E)** Repeat fasting glucose in 3 months

Answer

Correct answer : Arrange oral glucose tolerance test

This patient has impaired fasting glucose according to the IDF criteria with a glucose at or above 6.1 mmol/l and below 7.1 mmol/l. The recommendation would be for an OGTT with up to 30% of such cases having a diagnosis of diabetes on OGTT. He may have the metabolic syndrome although we are not told his waist circumference which is a criterion measurement.

Question 100

A 60 year old male with a 10 year history of type 2 diabetes was referred by his GP for conversion to insulin. He was taking metformin 850 mg tds, gliclazide 160 mg bd and pioglitazone 45 mg od. He does not smoke and denies any alcohol consumption.

On examination, his BMI is 41.2 kg/m^2, blood pressure 142/68 mmHg and abdominal examination reveals a 2 cm smooth non-tender hepatomegaly.

In type 2 diabetes, elevations of which liver enzymes are most correlated with non-alcoholic fatty liver disease?

- **A)** AST alone
- **B)** ALT and AST
- **C)** ALT and gamma-GT
- **D)** AST and gamma-GT
- **E)** gamma-GT and alkaline phosphatase

Answer

Correct answer : ALT and gamma-GT

Up to 20% of patients with T2DM have changes of fatty liver. Elevated concentrations of ALT more than AST (unlike alcoholic liver disease where AST is usually higher) is typical and gamma-GT is usually moderately elevated. Bilirubin and alkaline phosphatase are usually normal.

Question 101

An Asian lady with previous history of gestational diabetes presents around 16 week pregnant in antenatal clinic. She is otherwise asymptomatic and her pregnancy is progressing normally. According to NICE guidelines, what is the most appropriate time for her gestational diabetes mellitus (GDM) screening?

- **A)** As early as possible
- **B)** At 24 weeks
- **C)** At 28 weeks
- **D)** At 36 weeks
- **E)** No indication to check for GDM

Answer

Correct answer : As early as possible

According to NICE guidelines on gestational diabetes (NICE clinical guidelines 63), the following groups of patients should be screened for GDM:

- Previous history of GDM
- Certain ethnic groups (e.g. south east Asians, black Caribbean and middle eastern)
- Previous birth weight of a child > 4.5 Kg
- Body mass index > 30 kg/m^2
- Family history of a first degree relative with GDM

Screening for GDM in the above mentioned high risk group patients should be arranged at the booking appointment.

Question 102

Which of the following oral hypoglycemic agents is associated with vitamin B12 deficiency?

- **A)** Acarbose
- **B)** Gliclazide
- **C)** Glibenclamide
- **D)** Metformin
- **E)** Pioglitazone

Answer

Correct answer : Metformin

Long term metformin use has been linked with vitamin B12 deficiency according to results of a multicenter randomised, placebo controlled trial published in BMJ (online publication on May 20, 2010), although the mechanism for the deficiency remains unclear. It has been suggested that patients being initiated on long term metformin therapy should receive dietary counselling on starting the therapy and then randomised to systemic serum B12 screening or routine care groups for follow up purposes, as a cost effective measure.

Question 103

What is the risk of type I diabetes mellitus in a baby born to a mother with type 1 diabetes mellitus?

- **A)** <1%
- **B)** 1-2%
- **C)** 3-4%
- **D)** 5-10%
- **E)** 20-25%

Answer

Correct answer : 1-2%

The following table sums up the risk of development of Type 1 diabetes in a child with family history of Type 1 diabetes:

Type of DM	Type 1
Concordance In Monozygotic twins	36 %
Mother Diabetic	1-2% chance of having Type 1 DM

Question 104

According to the NICE lipid guidelines CG181, which of the following QRISK2 10 year risk predictions of cardiovascular disease should be the threshold for the introduction of statin therapy in a 45 year old man with type 2 diabetes?

- **A)** There is no threshold risk; the patient should be treated with a statin
- **B)** 5%
- **C)** 10%
- **D)** 15%
- **E)** 20%

Answer

Correct answer : 10%

According to the NICE guidelines, patients should be considered to be at high risk for cardiovascular disease if one or more of the following are present:

- Increased BMI
- Hypertension (> 140/80 mm of Hg)
- Microalbuminuria
- Smoker
- Deranged lipid profile
- Past medical history of cardiovascular disease
- Family history of cardiovascular disease

A cardiovascular risk of >10% on QRISK2 warrants therapy with statin therapy (atorvastatin as recommended by NICE).

Question 105

What is the chronology of appearance of hypoglycemic symptoms?

- **A)** Autonomic symptoms - Counterregulatory hormones - Neuroglycopenia
- **B)** Autonomic symptoms - Neuroglycopenia - Counter-regulatory hormones
- **C)** Counter regulatory hormones - Autonomic symptoms - Neuroglycopenia
- **D)** Counter regulatory hormones - Neuroglycopenia -autonomic symptoms
- **E)** Neuroglycopenia - Counter-regulatory hormones - Autonomic symptoms

Answer

Correct answer : Counter regulatory hormones - Autonomic symptoms - Neuroglycopenia

A fall in plasma glucose level evokes a rapid response by the body and includes the following steps:

- Release of counter-regulatory hormones such as glucagon, cortisol and growth hormones takes place at a plasma glucose level of < 3.8 mmol/L. These hormones induce gluconeogenesis and glycogenolysis to bring up the plasma glucose level
- Autonomic symptoms including tremors, anxiety, sweating and palpitations appear when the plasma glucose level falls below 3.4 mmol/L, as a result of increased sympathetic nervous system activity (the symptom of hunger is evoked due to parasympathetic nervous system activation).
- Neuroglycopenic symptoms are evoked when plasma glucose levels fall below 2.6 mmol/L and include confusion, lethargy, incoordination and blurred vision. A further decline in blood sugar or a lack of counter-regulatory response may result in loss of consciousness, convulsions and coma.

Question 106

A 64 year old type 2 diabetic is reviewed in clinic with poor glycemic control. She is currently on basal bolus insulin regimen comprising of 12 units of aspart insulin three times a day and 22 units of glargine insulin at night time. She is using an injectable device with which she is having trouble injecting, being aware that often the insulin is oozing out of the injection site. What is the most appropriate advice to improve her glycemic control?

- **A)** Reduce insulin dose
- **B)** Refer for DAFNE
- **C)** Switch to insulin analogues
- **D)** Switch to pen device
- **E)** Switch to premix BD insulin

Answer

Correct answer : Switch to pen device

Clearly she is facing difficulties as far as injecting insulin is concerned with oozing of insulin from the injection site. In the first instance, her delivery device can be changed to pen device.

According to NICE guidelines on type 2 diabetes mellitus (NICE clinical guideline 87):

Reference:

- Education should be offered to a diabetic who requires insulin about using an injection device
- In diabetics with manual or visual disability, an appropriate device or adaptation should be offered
- Appropriate local arrangements should be in place for disposal of sharps

Question 107

A 28 year old woman is diagnosed with gestational diabetes in her first pregnancy. She is treated with metformin in the first instance. Which of the following is the appropriate advice regarding blood sugar monitoring according to guidance for this patient?

- **A)** Check blood sugars before every meal
- **B)** Check fasting and 2-hours post meal blood sugars
- **C)** Check fasting and 1-hour post prandial blood sugars
- **D)** Check blood sugars twice a day
- **E)** Check blood sugar every alternate day

Answer

Correct answer : Check fasting and 1-hour post prandial blood sugars

According to NICE guidance, women with gestational diabetes who are being treated with lifestyle advice or oral therapy are advised to test fasting and 1-hour postprandial blood glucose levels after every meal.

Question 108

A 55 year old, Type 2 diabetic, on a basal bolus insulin regimen, recently lost blood through an episode of haematemesis, with a fall in the haemoglobin concentration of 2.5 g/l. He is reviewed in the diabetic clinic, where it is noticed that his home blood sugar readings are mostly 8-14 mmol/L. While his HbA1C value as checked in diabetic clinic is 47.5 mmol/mol (6.5%).

What is the next best step in his management?

- **A)** Decrease his insulin dose
- **B)** Educate him regarding blood sugar monitoring technique
- **C)** Increase his insulin dose
- **D)** No change required
- **E)** Recheck his HbA1C in 6-8 weeks time

Answer

Correct answer : Increase his insulin dose

Falsely low values of HbA1C are associated with haemoglobinopathies (such as Hb C, D and S) and reduced survival of RBC secondary to haemolysis or haemorrhage. This gentleman has suboptimal glycaemic control as reflected by his home blood sugar readings but his HbA1C is inappropriately low as a result of recent blood loss. As a result his insulin dose needs to be increased to control impaired home blood sugar readings.

In contrast falsely elevated HbA1c values can be seen in uraemia (carbamylated Hb) or in presence of Hb F.

Question 109

An 18 year old presents with symptoms of weight loss, polyuria and polydipsia. On examination he has optic atrophy and sensori neural deafness. He has a strong family history of diabetes mellitus and sensorineural deafness. His biochemical investigations reveal high blood sugars and glycosuria. What should be the next investigation to further establish the diagnosis of his underlying familial condition?

- **A)** Anti-GAD antibodies
- **B)** Bone profile
- **C)** CT abdomen
- **D)** Prolactin
- **E)** Screen for Diabetes insipidus

Answer

Correct answer : Screen for Diabetes insipidus

This 18 year old is likely to have Wolfram's syndrome (DIDMOAD) , which is a rare genetic disorder associated with non immune mediated pancreatic ß-cell destruction, diabetes insipidus, optic atrophy and neural deafness. The affected individuals have abnormalities in the process of myelination and mitochondrial malfunction. The life expectancy of affected individuals is about 3 decades.

Question 110

A 44 year old gentleman with a body mass index of 47 kg/m^2 presents to the clinic with poorly controlled Type 2 DM. He has multiple co-morbidities including sleep apnoea, hypertension and osteoarthritis.

According to NICE guidelines what is the next best step in his management?

- **A)** Bariatric surgery
- **B)** Exenatide
- **C)** Insulin
- **D)** Orlistat
- **E)** Topiramate

Answer

Correct answer : Bariatric surgery

According to NICE guidelines on management of overweight and obese adults (NICE clinical guidelines 43), consider surgery for people with severe obesity if:

- They have a BMI of 40 kg/m2 or more, or between 35 kg/m2 and another significant disease (for example, type 2 diabetes, high blood pressure) that could be improved if they lost weight
- All appropriate non-surgical measures have failed to achieve or maintain adequate clinically beneficial weight loss for at least 6 months
- They are receiving or will receive intensive specialist management
- They are generally fit for anaesthesia and surgery
- They commit to long term follow up
- Consider surgery as a first line option for adults with a BMI > 50 kg/m2 in whom surgical intervention is considered appropriate; consider orlistat before surgery if the waiting time is long

Question 111

A 25 year old woman with a 7 year history of type 1 diabetes presents to clinic being 8 weeks pregnant. Her glycaemic control has been excellent with a HbA1c of around 42.1- 47.5 mmol/mol (6-6.5%) on basal bolus insulin. She enquiries about a possible risk of major congenital malformations in her offspring.

What are the chances of major congenital malformation in her child?

- **A)** <1%
- **B)** 1%
- **C)** 5-7%
- **D)** 10%
- **E)** Same as background population

Answer

Correct answer : Same as background population

The risk of congenital abnormalities and perinatal mortality is increased in babies born to diabetic mothers by two- folds and three -folds respectively. Good glycaemic control around conception and early pregnancy can reduce the incidence of both the above mentioned complications. The major congenital abnormalities detected in neonates include congenital heart disease (x3.4 times higher risk) and neural tube defects (x3-4 times higher risk) (1). According to the results from The Diabetes Control and Complications Trial (DCCT) good glycaemic control is associated with rates of spontaneous abortion and congenital malformations similar to those seen in the non-diabetic population (2).

Reference:

1. Perinatal mortality and congenital anomalies in babies of women with Type 1 or Type 2 Diabetes in England, Wales and Northern Ireland: population based study by Macintosh et al., BMJ 2006;333:177(22 July)
2. Pregnancy outcomes in the Diabetic Control and Complication Trial - Am J Obstetrics and Gynaecology, 1996 Apr;174(4):1343-53

Question 112

According to NICE, which of the following is a target range for blood glucose during pregnancy?

- **A)** 1 hour postprandial <7.8 mmol/l
- **B)** 1 hour postprandial <9 mmol/l
- **C)** 2 hour postprandial <7.8 mmol/l
- **D)** 2 hour postprandial <9 mmol/l
- **E)** Fasting plasma glucose <5.5 mmol/l

Answer

Correct answer : 1 hour postprandial <7.8 mmol/l

In accordance with NICE guidelines (February 2015):
Advise pregnant women with any form of diabetes to maintain their capillary plasma glucose below the following target levels, if these are achievable without causing problematic hypoglycaemia: fasting: 5.3 mmol/litre and 1 hour after meals: 7.8 mmol/litre or 2 hours after meals: 6.4 mmol/litre
Advise pregnant women with diabetes who are on insulin or glibenclamide to maintain their capillary plasma glucose level above 4 mmol/litre.

Question 113

According to NICE guidelines, in women with gestational DM, (who are on dietary control/oral hypoglycaemic agent) what are the recommendations regarding frequency of blood sugar monitoring?

- **A)** Every 4 hourly
- **B)** Fasting and 2 hour postprandial
- **C)** Fasting and 1 hour postprandial
- **D)** Fasting and before every meal
- **E)** Once a day

Answer

Correct answer : Fasting and 1 hour postprandial

According to current NICE guidelines for the management of diabetes during pregnancy (February 2015), advise pregnant women with type 2 diabetes or gestational diabetes -who are on a multiple daily insulin injection regimen to test their fasting, pre-meal, 1-hour post-meal and bedtime blood glucose levels daily during pregnancy.

Advise pregnant women with type 2 diabetes or gestational diabetes to test their fasting and 1-hour post-meal blood glucose levels daily during pregnancy if they are on diet and exercise therapy or taking oral therapy (with or without diet and exercise therapy) or single-dose intermediate-acting or long-acting insulin.

Question 114

A 32 year old woman with gestational diabetes in her second pregnancy treated with twice daily insulin delivers a healthy child via vaginal delivery. Post delivery her blood glucose concentrations quickly revert to normal and she no longer requires insulin. Which of the following applies regarding postpartum screening for diabetes in this woman?

- **A)** Arrange for a fasting blood glucose 6 weeks post delivery
- **B)** Arrange for an OGTT 6 weeks post delivery
- **C)** Arrange for an OGTT 3 months post delivery
- **D)** Arrange postprandial glucose measurement 6 weeks post delivery
- **E)** Check HbA1c 6 weeks postpartum

Answer

Correct answer : Arrange for a fasting blood glucose 6 weeks post delivery

In accordance with NICE Clinical Guidelines 63, women who were diagnosed with gestational diabetes should be offered lifestyle advice (including weight control, diet and exercise) and offered a fasting plasma glucose measurement (but not an OGTT) at the 6-week postnatal check and annually thereafter. Women who were diagnosed with gestational diabetes (including those with ongoing impaired glucose regulation) should be offered early self-monitoring of blood glucose or an OGTT in future pregnancies. A subsequent OGTT should be offered if the test results in early pregnancy are normal.

Reference:

NICE CG63: diabetes in pregnancy

Question 115

A 25 year old male is recently diagnosed as having diabetes mellitus (DM) based on routine screening. His BMI is 24 kg/m^2 and there are no ketone bodies in urine with only 2+ sugars. His recent ultrasound abdomen did not show any abnormalities. He has a strong family history of type 2 DM with few of the family members requiring insulin therapy for control. What's the likely underlying genetic mutation?

- **A)** Glucokinase
- **B)** HNF 1α
- **C)** HNF 4α
- **D)** IPF
- **E)** NeuroD1

Answer

Correct answer : HNF 1α

The patient is likely to have MODY type 3, caused by mutation of hepatocyte nuclear factor-1α, located on chromosome 12. It is the commonest type of maturity onset diabetes of the young, accounting for approximately 70% of all the MODY. It is characterised by severe hyperglycaemia and about one third of patients require insulin therapy for control of diabetes. Early on in the disease patients may display an exaggerated response to sulphonylurea therapy.

Question 116

A 25 year old man of Caucasian origin was recently diagnosed to have Diabetes and started on insulin therapy. In last 6 weeks he is having multiple episodes of hypoglycaemia and his insulin requirement has reduced to 12 units per day.

His clinical examination is normal and he has a body mass index of 22kg/m^2. A recent renal scan had shown presence of renal cysts. He has a strong family history of Diabetes with his father and 3 first cousins developing diabetes in their 3rd to 4th decade.

Which of the following test is likely to reveal his underlying diagnosis?

- **A)** Anti GAD antibodies
- **B)** Anti islet cells antibodies
- **C)** Insulin, C peptide levels
- **D)** Renin levels
- **E)** Screening for monogenetic diabetes

Answer

Correct answer : Screening for monogenetic diabetes

The patient has MODY 5, which is secondary to mutation of HNF-1Beta and is characterised by onset of diabetes in the third decade and association with renal cysts or uterine abnormalities in females.

Question 117

A 55 year old man with type 2 Diabetes is reviewed in the clinic. His biochemistry results are as shown:

		Normal Ranges
Albumin	38 g/L	(30-50 g/L)
ALP	175 U/L	(50-125 U/L)
ALT	125 mU/L	(05-58 U/L)
Bilirubin	35 micromol/L	(0-18)
Proteins	66 g/L	(60-80 g/L)
Ferritin	550 pmol/L	(10-300 ng/mL)
Transferrin saturation	52%	(15-50%)
HbA1c	66.1 mmol/mol (8.2%)	(< 42.1 mmol/mol (6))
Hb	12.8 g/L	(12-16)

Which of the following is the likely underlying diagnosis?

- **A)** Glycogen storage disease
- **B)** Haemochromatosis
- **C)** LADA
- **D)** Mitochondrial disease
- **E)** MODY

Answer

Correct answer : Haemochromatosis

Haemochromatosis (Bronze diabetes) is a hereditary (HFE/haemojuvelin/hepcidin and other gene mutations) or acquired (e.g. secondary to repeated blood transfusions) condition leading to pathological effects of iron accumulation on multiple organs and can present with one or more of the following features:

- Deranged LFT/cirrhosis
- Diabetes due to pancreatic ß cell failure
- Hypogonadism
- Skin pigmentation
- Cardiomyopathy
- Arthritis

Question 118

A 45 year old man with type 2 DM for 8 years presents to clinic with a lack of libido and erectile dysfunction. His BMI is 36 kg/m^2 and there is no loss of secondary sexual characteristics. He denies usage of any substance of abuse and his alcohol intake is 14 units in a week. His biochemistry shows:

		Normal Ranges
FSH	2.2 U/L	(1-10)
LH	3.5 U/L	(3-10)
Testosterone	7.5 nmol/L	(9-28.5)
Prolactin	350 mU/L	(45-400)
ALT	60 u/l	(0-40)

He undergoes MRI which shows no obvious abnormality. His serum transferrin saturations were normal.What is the likely explanation for his low libido?

- **A)** Anabolic steroid usage
- **B)** Haemochromatosis
- **C)** Kallmann syndrome
- **D)** Klinefelter's syndrome
- **E)** Obesity

Answer

Correct answer : Obesity

Erectile dysfunction is defined as the inability to achieve or maintain an erection for sufficient time, duration and firmness resulting in incomplete sexual activity in > 25% of the attempts. About 10% of men are affected by low libido and erectile dysfunction and the prevalence increases with age.

The following is a list of main causes for erectile dysfunction:

- Medications such as diuretics, ß blockers, MAO inhibitors, opioids, glucocorticoids, tranquilizers, digoxin, antiandrogens, gemfibrozil
- Systemic illness (heart failure, cirrhosis, uraemia etc.)
- Neurological conditions such as autonomic neuropathy, cord compression
- Vascular conditions such a peripheral vascular disease
- Endocrine disease (hypogonadism, diabetes, thyroid dysfunction)
- Psychological
- Urogenital abnormalities like trauma, priapism and Peyronie`s disease
- Alcohol, substance of abuse like heroin, marijuana

This gentleman has features of secondary gonadal failure as evidenced by low testosterone and low FSH/LH levels. His age group and normal secondary sexual characteristics make it unlikely for him to have any genetic abnormality like Kallmann syndrome. A normal MRI rules out any structural pituitary or hypothalamic disease. He is not on any medication and is systemically well. A slightly elevated ALT is common in obese individuals due to fatty infiltration. A transferrin saturation makes it unlikely for him to have haemochromatosis. Obese individuals have increased activity of aromatase which converts testosterone to oestrogens which in turn suppress FSH/LH levels. Total testosterone concentrations are influenced by sex hormone-binding globulin (SHBG) concentrations, which are decreased by obesity and increased with ageing.

Question 119

A 65 year old male diabetic presents with a superficial ulcer under the second toe of the right foot. He has been on antibiotics for the last 2 weeks and the discharge from the ulcer is clean. His HbA1C is 50.8 mmol/mol (6.8%) and medications include aspirin, clopidogrel, ramipril, amlodipine, simvastatin, pregabalin and pentoxifylline. On examination, his dorsalis pedis pulse is feebly palpable.

Which of the following is the most appropriate step in his management?

- **A)** Continue the antibiotics
- **B)** Debride the ulcer
- **C)** Improve glycaemic control
- **D)** Silver containing dressing
- **E)** Vascular review

Answer

Correct answer : Vascular review

This gentleman has a satisfactory glycaemic control as reflected by HbA1C of 50.8 mmol/mol (6.8%). His ulcer seems to have responded to antibiotic therapy as evidenced by a clear serous discharge from the ulcer and the superficial nature of the ulcer makes debridement a less attractive option. As he has evidence of peripheral vascular disease (taking pentoxifylline tablets), he should be referred for a vascular review to assess if the blood flow to the extremity could be improved.

According to the NICE guidelines regarding management of diabetic foot ulcer (NICE clinical guideline 10), examination of a patient's feet should include;

- Testing of foot sensation using a 10 g monofilament or vibration
- Palpation of foot pulses
- Inspection of any foot deformity and footwear

The foot risks are classified as:

- At low risk (need annual review)
- At increased risk: in the presence of peripheral neuropathy or vascular insufficiency (arrange regular review at 3-6 monthly interval, by the foot protection team)
- At high risk: in the presence of peripheral neuropathy or vascular insufficiency along with deformity or previous ulcer or skin change (arrange frequent review; 1-3 monthly)
- Foot care emergencies including new ulceration, swelling or discolouration (review by multidisciplinary foot care team within 24 hours)

Question 120

A 25 year old man with type 1 diabetes is reviewed in clinic. He is currently on basal bolus insulin therapy. His home blood sugar readings are generally high (>10 mmol/mol). He has not suffered from any hypoglycaemic episodes in the last 1 year. According to NICE guidelines, what is the cut off value for HbA1C in patients with type 1 diabetes mellitus for use of insulin pumps?

- **A)** > 58.5 mmol/mol (7.5%)
- **B)** > 63.9 mmol/mol (8.0%)
- **C)** > 69.5 mmol/mol (8.5%)
- **D)** > 74.9 mmol/mol (9.0%)
- **E)** > 80.3 mmol/mol (9.5%)

Answer

Correct answer : > 69.5 mmol/mol (8.5%)

According to NICE guidelines insulin pump therapy should be considered in type 1 diabetics who are DAFNE trained and are on basal bolus insulin regimen if their glycaemic control remains unsatisfactory HbA1C > 69.5 mmol/mol (8.5%) or they are having frequent hypoglycaemic episodes.

Question 121

A 45 year old type 2 diabetic male is referred with episodes of epigastric pain and nausea for the last few weeks. His blood test results were as detailed below:

		Normal Ranges
Albumin	35 g/L	(30-50)
ALP	72 U/L	(50-125)
ALT	41 mU/L	(5-58)
Bilirubin	10 micromol/L	(0-18)
Proteins	64 g/L	(60-80)
FT_4	18.4 pmol/L	(9-23)
TSH	1.1 mU/L	(0.35-5.5)
LDL	2.5 mmol/L	(<3)
Total Cholesterol	4.4 mmol/L	(<5)
Triglycerides	16.3 mmol/L	(1.1-2)
HbA1C	54.1 mmol/mol (7.1%)	(<42.1 mmol/mol (6))

Which lipid lowering agent should be started in his case?

- **A)** Atorvastatin
- **B)** Ezetimibe
- **C)** Fenofibrate
- **D)** Niaspan
- **E)** Rosuvastatin

Answer

Correct answer : Fenofibrate

According to the NICE guidelines on type 2 diabetes (NICE clinical guideline 87), a type 2 diabetes mellitus patient with high serum triglyceride (TG) levels should be initially assessed for a possible secondary cause of hypertriglyceridaemia (including poorly controlled diabetes, hypothyroidism, Cushing's syndrome, chronic renal failure, drugs such as steroids, oestrogens, isotretinoin) and treated if such a cause is identified. If the TG levels remain elevated then fibrates should be offered. These may be started before the statin in a scenario of acute need (e.g. impending pancreatitis). If lifestyle measures and fibrates are ineffective in controlling TG levels a trial of omega-3 fish oils is recommended.

Question 122

A 21 year old male shift worker, who has been a diabetic for 14 years, presents with recurrent episodes of hypoglycaemia. He is taking 12 units of short acting insulin analogue (insulin aspart) three times a day and on 22 units of long acting insulin analogue (glargine insulin). His home blood sugar monitoring shows blood sugar values varying from 2-20. What is the next most appropriate step in his management?

- **A)** Acarbose
- **B)** Decrease his insulin dose
- **C)** Metformin
- **D)** Refer to a course on carbohydrate counting (DAFNE)
- **E)** Start him on an insulin pump

Answer

Correct answer : Refer to a course on carbohydrate counting (DAFNE)

This 21 year old has suboptimal glycaemic control and massive fluctuations in his blood sugar values, despite being on an intensive basal bolus insulin regimen. As he works in a shift pattern the fluctuations in blood sugar readings can be improved if he varies his short acting insulin dose depending upon the carbohydrate content of the meal. If these measures are not helpful, he should be referred for continuous subcutaneous insulin infusion (CSII).

Question 123

A 38 year old type 1 diabetic female, who has been on insulin pump for last 6 months, presents to clinic with recurrent hypoglycaemic episodes. She confesses that she is not checking her blood sugars and does not maintain a calorie intake diary. The pump also has come out on numerous occasions while she is asleep. What is the most appropriate step in her management?

- **A)** Dietary advice
- **B)** Intensify the control
- **C)** Remove insulin pump
- **D)** Replace the tubing of pump
- **E)** Offer more education about insulin pump use

Answer

Correct answer : Offer more education about insulin pump use

This lady is on insulin pump and her glycaemic control is suboptimal, reflecting a lack of monitoring and awareness on her part. In this case it is so important to get this woman to understand the importance of glycaemic control and adherence to the pump. She should be offered further education regarding carbohydrate counting, regular blood sugar monitoring and adjustment of the insulin pump basal rate.

Question 124

A 49-year old barrister with a 2 year history of type 2 diabetes mellitus, controlled on diet, attends clinic asking to be prescribed metformin. She has a family history of colorectal cancer, which has affected both her parents and a maternal aunty. She has read an article that metformin may be protective against cancer in diabetes.
Which of the following is correct?

- **A)** There is no evidence to suggest that metformin is protective against colorectal cancer.
- **B)** Metformin reduces the risk of bowel adenocarcinoma but not squamous cell carcinoma.
- **C)** Metformin in combination with gliclazide reduces the risk of colorectal cancer by a factor of 1.8.
- **D)** Metformin activates adenosine monophosphate-activated protein kinase, which may suppress tumour formation.
- **E)** Metformin has been shown in vitro to inhibit the effects of tumour suppressor genes such as p53.

Answer

Correct answer : Metformin activates adenosine monophosphate-activated protein kinase, which may suppress tumour formation.

Metformin may have a protective effect against cancer and pilot studies from a diabetes database support this. The potential mechanism is that metformin activates adenosine monophosphate-activated protein kinase which may suppress tumour formation.

Question 125

A 57-year old petro-chemical engineer attends diabetes clinic having recently been diagnosed with type 2 diabetes. She has spent most of her working life exposed to benzene derivatives. Aged 49 she was diagnosed with breast cancer, which was treated with a lumpectomy. Her husband is undergoing chemotherapy for disseminated colorectal cancer.

She has read in a Sunday magazine that diabetes may be associated with an increased risk of cancer and asks for your opinion on this article. What do you advise?

- **A)** She should not believe what she reads in the Sunday press?
- **B)** Type 2 diabetes is associated with a greater incidence of cancer, particularly of the pancreas, breast and colon.
- **C)** Type 2 diabetes is associated with a greater incidence of cancer, particularly of the pancreas, lung and brain.
- **D)** The risk of bowel, breast and pancreatic cancer in type 2 diabetes is 1.6 times greater than that for type 1 diabetes.
- **E)** The risk of bowel, breast and pancreatic cancer is 3 times more common in type 2 diabetes than type 1 diabetes.

Answer

Correct answer : Type 2 diabetes is associated with a greater incidence of cancer, particularly of the pancreas, breast and colon.

The greater incidence of breast, pancreatic and colon cancer in patients with type 2 diabetes may be multifactorial, possibly linked to obesity, insulin resistance or hyperglycaemia. For example, carcinoma of the colon is associated with obesity, hyperglycaemia, metabolic syndrome, hypertriglyceridaemia, insulin treatment and raised insulin-like growth factor levels.

Question 126

You have recently started a 61 year old teacher with a 5 year history of type 2 diabetes on exenatide. Her colleague at school also has type 2 diabetes and is on liraglutide and has told her it is “better than exenatide.” The patient contacts you asking for your advice on this as she is keen to change to liraglutide. How do you advise her?

- **A)** Liraglutide has demonstrated non-inferiority compared to exenatide.
- **B)** In a head-to-head comparative study against exenatide, liraglutide was associated with a 0.3% superior HbA1c reduction.
- **C)** In a head-to-head comparative study against exenatide, liraglutide was associated with a 0.9% superior HbA1c reduction.
- **D)** In an open-labelled study exenatide has demonstrated a 0.4% superior HbA1c reduction compared to liraglutide.
- **E)** Exenatide has demonstrated non-inferiority compared to liraglutide.

Answer

Correct answer : In a head-to-head comparative study against exenatide, liraglutide was associated with a 0.3% superior HbA1c reduction.

In comparative studies, liraglutide has demonstrated superior HbA1c reductions compared to glimepiride, metformin, rosiglitazone, and insulin glargine. In a head-to-head comparative study against exenatide, liraglutide was associated with superior HbA1c reductions of 0.3%.

Question 127

A 58 year old patient with a 14 year history of type 2 diabetes (T2DM) presents to clinic. His HbA1c is 125.1 mmol/mol (13.6%) despite taking metformin 1 g bd., gliclazide 160 mg bd., and exenatide 10 mcg bd. His BMI is 35 kg/m^2, his blood pressure is 164/98 mmHg and he has pre-proliferative retinopathy, microalbuminuria, and a distal sensorimotor neuropathy.

He refuses to consider insulin therapy and is not keen on attending a recommended EXPERT patient education programme as he doesn't like talking to other "diabetics". You diagnose him with 'Ppsychological insulin resistance.'

Which factor constitute psychological insulin resistance?

- **A)** A perceived loss of control over one's life; poor self-efficacy; anxiety; perceived disease severity; injection related anxiety; a perceived lack of positive gain.
- **B)** A perceived loss of control over one's life; neurosis; personal failure; perceived disease severity; injection related anxiety; a perceived lack of positive gain.
- **C)** A perceived loss of control over one's life; poor self-efficacy; personal failure; perceived disease severity; injection related anxiety; a perceived lack of positive gain.
- **D)** A perceived loss of control over one's life; poor self-efficacy; personal failure; perceived disease severity; injection related anxiety; depression.
- **E)** A perceived loss of control over one's life; poor self-efficacy; hysteria; perceived disease severity; injection related anxiety; a perceived lack of positive gain.

Answer

Correct answer : A perceived loss of control over one’s life; poor self-efficacy; personal failure; perceived disease severity; injection related anxiety; a perceived lack of positive gain.

Patients with T2DM are often reluctant to begin insulin and, in many cases, delay the start of insulin therapy for quite lengthy periods of time. This has led to the development of the concept of “psychological insulin resistance” (PIR).

While clinical lore suggests that PIR is quite common, there has been little formal study in this area. In the United Kingdom Prospective Diabetes Study (UKPDS), of those with T2DM randomized to insulin therapy, 27% initially refused. Early reports from the international Diabetes Attitudes, Wishes, and Needs (DAWN) study indicate that the majority (54.9%) of insulin-naïve patients worry about the possibility of insulin therapy. The six features of PIR are as listed in answer C, which is the best answer.

Question 128

A 45-year old builder with a 12 year history of type 2 diabetes has an HbA1c of 102.2 mmol/mol (11.5%) despite taking metformin 1 g bd., gliclazide 160 mg bd., and sitagliptin 100 mg od. He has refused exenatide or insulin due to a needle phobia.

According to research on the concept of ‘psychological insulin resistance’ what percentage of patients who are reluctant to start insulin have a needle phobia?

- **A)** 10%
- **B)** 40%
- **C)** 50%
- **D)** 60%
- **E)** 80%

Answer

Correct answer : 50%

The fifth factor in the concept of psychological insulin resistance (PIR) concerns injection related anxiety. Approximately 50% of patients report being fearful of injections. Although this is often presumed to be the single, or single largest, contributor to PIR, it may be overstated. True injection phobia is rare, even among insulin-using patients with diabetes.

Question 129

A 72 year old American tourist with a 4 year history of type 2 diabetes is admitted to the acute assessment unit with haematemesis. The House-Officer / Foundation Year 1 doctor admits the patient and erroneously informs you that the management of the patient's diabetes is ‘diet-control’.

Upon reviewing the drug chart you note the patient is on bromocriptine. How can bromocriptine be used in the management of type 2 diabetes?

- **A)** By inhibiting central D2 receptors bromocriptine increases systemic insulin sensitisation.
- **B)** By reducing serum prolactin levels bromocriptine augments the effects of endogenous incretins on reducing satiety and slowing gastric emptying.
- **C)** Body fat stores and insulin action are controlled by the temporal interaction of circadian neuroendocrine oscillations. Bromocriptine modulates neurotransmitter action in the brain and is associated with HbA1c reductions of 0.56%.
- **D)** Hyperprolactinaemia is associated with type 2 diabetes and by treating hyperprolactinaemia plasma glucose levels improve.
- **E)** Bromocriptine reduces glucagon secretion.

Answer

Correct answer : Body fat stores and insulin action are controlled by the temporal interaction of circadian neuroendocrine oscillations. Bromocriptine modulates neurotransmitter action in the brain and is associated with HbA1c reductions of 0.56%.

Body fat stores and insulin action are controlled by the temporal interaction of circadian neuroendocrine oscillations. Bromocriptine modulates neurotransmitter action in the brain. Studies using bromocriptine in type 2 diabetes have shown improvements in glycaemic control and glucose tolerance with HbA1c reductions of ~0.56%.

Despite receiving FDA approval, bromocriptine is not part of the type 2 diabetes management guidelines from the National Institute for Health and Clinical Excellence. It is commonly used in the management of T2DM in the USA.

Question 130

A 40 year old lady with a 2 year history of type 2 diabetes is reviewed in diabetes clinic in the summer. Six months prior to this appointment, during the winter, your colleagues started her on sitagliptin 100 mg o.d.

The patient has a past medical history of eczema, asthma and perennial rhinitis. She comments that since she started sitagliptin she has noticed a ‘blocked and stuffy’ sensation in her nose and throat.

What do you advise?

- **A)** Her symptoms are most likely related to hay fever in the summer months.
- **B)** Sitagliptin is associated with nasopharyngitis and may be contributory.
- **C)** She should be referred to an allergy clinic in view of her past medical history of atopy.
- **D)** She should be prescribed an antihistamine and nasal decongestants.
- **E)** She should monitor her PEFR twice daily as her asthma may have decompensated.

Answer

Correct answer : Sitagliptin is associated with nasopharyngitis and may be contributory.

Several selective inhibitors of DPP-4 have been developed and those that are licensed include sitagliptin, vildagliptin, and more recently, saxagliptin. They offer an alternative oral treatment for T2DM, which unlike the sulphonylureas, are not associated with hypoglycaemia or weight gain. They achieve a 0.4-0.7% HbA1c reduction over 12 months.

Adverse effects include nasopharyngitis, urinary tract infections and pancreatitis.

Question 131

You review a 55 year old male patient with a 12 year history of type 2 diabetes. He is on metformin 1g b.i.d., gliclazide 160 mg b.i.d., and pioglitazone 30mg o.d. His BMI is 36 kg/m^2. You consider adding in exenatide. The patient is concerned that exenatide may increase the risk of hypoglycaemia.

What do you advise?

- **A)** Exenatide acts in a glucose independent manner. Therefore there is a high risk of hypoglycaemia.
- **B)** The risk of hypoglycaemia is increased in patients on exenatide who are also taking a sulphonylurea.
- **C)** The risk of hypoglycaemia is increased in patients on exenatide who are also taking metformin.
- **D)** The risk of hypoglycaemia is increased in patients on exenatide who are also taking a thiazolidinedione.
- **E)** The risk of hypoglycaemia in decreased if exenatide is administered one hour before oral hypoglycaemic agent therapy.

Answer

Correct answer : The risk of hypoglycaemia is increased in patients on exenatide who are also taking a sulphonylurea.

The most common side-effects associated with exenatide include nausea and vomiting. They are dose-dependent and more common during drug initiation but subside over time. The risk of hypoglycaemia is increased in patients on exenatide who are also taking a sulphonylurea.
In contrast, the risk of hypoglycaemia is not increased when exenatide is combined with metformin or a thiazolidinedione.

Question 132

You review a 22 year old lady who was found to have a fasting blood glucose of 15 mmol/L, which when repeated was 14.5 mmol/L. Her 21 year old sister was recently diagnosed with diabetes and her 24 year old brother was diagnosed with diabetes aged 22.

You look back through her medical records and note that she has a history of pelvic inflammatory disease. A urinary chlamydia antigen test was positive. An ultrasound scan of her pelvis was reported as showing bilateral renal cysts and a unicornuate uterus. She also has a history of gout and is known to binge drink.

What is the underlying diagnosis.

- **A)** Type 1 diabetes
- **B)** Polycystic ovarian syndrome
- **C)** MODY 1
- **D)** MODY 3
- **E)** MODY 5

Answer

Correct answer : MODY 5

MODY 5 is due to a mutation in HNFi1ß and accounts for 3% of cases of MODY. The average age of presentation is 22 years associated with renal cysts often with uterine abnormalities, gout and insulin resistance.

Question 133

A 25 year old model with a 17 year history of type 1 diabetes presents to clinic concerned about her fingernails. She has noticed an area of redness over her nail folds, which have been present for the last month. She is concerned as this may affect her employment prospects. What is the most likely diagnosis?

- **A)** Bullosis diabeticorum
- **B)** Diabetic thick skin
- **C)** Folliculitis
- **D)** ANCA negative small vessel vasculitis
- **E)** Periungual telangiectasia

Answer

Correct answer : Periungual telangiectasia

Skin conditions specific to diabetes include: pretibial diabetic dermopathy, bullosis diabeticorum, diabetic thick skin, and periungual telangiectasia. Periungual telangiectasia is characterised by venous capillary dilatation at the nail fold seen in up to 50% of people with diabetes. Note that necrobiosis lipoidica, vitiligo, and granuloma annulare are skin conditions seen more commonly in those with diabetes but are not specific to diabetes.

Question 134

A 42 year old patient with a 29 year history of type 1 diabetes presents to clinic. He works as a builder and operates heavy drilling machinery. He is concerned that the skin on his hands is thickening and feels tight. This has resulted in reduced joint mobility in his hands. He drinks 35 units of alcohol weekly. On examination you note that he is unable to place the palms of the hands flat together and make the ‘prayer sign.’ What is the most likely diagnosis.

- **A)** Dupuytren’s contracture.
- **B)** Diabetic cheiroarthropathy.
- **C)** Limited cutaneous scleroderma.
- **D)** Diabetic thick skin.
- **E)** Diabetic bullae.

Answer

Correct answer : Diabetic cheiroarthropathy.

Diabetes is associated with an increased incidence of pseudogout and osteoarthritis but the classical condition to consider is the ‘stiff hand syndrome’ or diabetic cheiroarthropathy. In this the skin thickens and tightens which, in association with sclerosis of the tendon sheaths, results in limited joint mobility in the hands and less commonly the feet. This reduced joint mobility gives an inability to place the palms of the hand flat together and make the ‘prayer sign.’ No specific treatment for this currently exists.

Question 135

Patients with T2DM are at increased risk of a large number of diabetes-related complications due to an unnecessary delay in insulin initiation. What is the average delay between starting oral hypoglycaemic therapy to initiating insulin?

- **A)** 2 years.
- **B)** 5 years.
- **C)** 8 years.
- **D)** 11 years.
- **E)** 15 years.

Answer

Correct answer : 11 years.

Recent data have shown that patients with T2DM in the UK delay initiating insulin on average for over 11 years after first being prescribed an oral medication. It was found that for patients immediately initiating insulin there were increases in (undiscounted) life expectancy of 0.61 years and quality-adjusted life expectancy of 0.34 quality-adjusted life years versus delaying initiation for 8 years. There were also substantial reductions in cumulative incidence and time to onset of all diabetes-related complications with immediate versus delayed insulin initiation.

Question 136

What percentage of patients do not achieve the target HbA1c of <53.0 mmol/mol (7%) recommended by the American Diabetes Association on oral hypoglycaemic agent therapy?

- **A)** 10%
- **B)** 20%
- **C)** 40%
- **D)** 60%
- **E)** 70%

Answer

Correct answer : 60%

Despite the availability of many anti-diabetic agents, approximately 60% of patients do not achieve the target HbA1C level of <53.0 mmol/mol (7%). Reasons for this include: noncompliance; side-effects of treatments; fear of hypoglycaemia; weight-gain; problems with dose titration of anti-diabetic agents; and more stringent HbA1C targets set by healthcare organisations which tend to change.

Question 137

You review a 45 year old ecologist who has been found to have fasting plasma glucose of 8.4 mmol/L and 9.1 mmol/L on two occasions. She has not lost weight and her GAD antibodies are negative. Her HbA1c is 56.3 mmol/mol (7.3%), her blood pressure is 130/78 mmHg and her BMI is 29 kg/m ^{2}.

You diagnose her with type 2 diabetes with the recommendation that she commences metformin 500 mg b.i.d. in the first instance. She refuses treatment preferring to use herbal medicines. She has read that karela supplements are of value in type 2 diabetes and would like to try them first.

How do karela supplements benefit patients with type 2 diabetes?

- **A)** Karela reduces peripheral insulin resistance.
- **B)** Karela inhibits hepatic gluconeogenesis.
- **C)** Karela inhibits free fatty acid oxidation.
- **D)** Karela has hypoglycaemic effects.
- **E)** Karela has incretin like effects.

Answer

Correct answer : Karela has hypoglycaemic effects.

The hypoglycaemic effects of karela are well documented. It is used traditionally in Asian cookery and as a traditional medicine to lower blood glucose levels. In practice it is difficult to take enough of the Karela plant to have a significant effect. karela capsules are an unknown entity. While certain components of karela do have hypoglycaemic effects there have been no formal studies to indicate if it can be used safely in capsule form by people with diabetes. Many natural products and herbal medicines are not safe when used in conjunction with other pharmaceutical medicines and can cause problems.

Question 138

A 72-year-old man is reviewed in the diabetes clinic. He has a history of heart failure and type 2 diabetes mellitus. His current medications include furosemide 40mg od, ramipril 10mg od and bisoprolol 5mg od. Clinical examination is unremarkable with no evidence of peripheral oedema, a clear chest and blood pressure of 130/76 mmHg. Recent renal and liver function tests are normal. Which one of the following medications is contraindicated?

- **A)** Exenatide
- **B)** Gliclazide
- **C)** Metformin
- **D)** Pioglitazone
- **E)** Sitagliptin

Answer

Correct answer : Pioglitazone

Thiazolidinediones are absolutely contraindicated in heart failure

Thiazolidinediones are a new class of agents used in the treatment of type 2 diabetes mellitus. They are agonists to the PPAR-gamma receptor and reduce peripheral insulin resistance. Thiazolidinediones are contraindicated in patients with heart failure or who are at high risk of bone fractures. Rosiglitazone was withdrawn in 2010 following concerns about the cardiovascular side-effect profile.

The PPAR-gamma receptor is an intracellular nuclear receptor. Its natural ligands are free fatty acids and it is thought to control adipocyte differentiation and function.

Adverse effects

- Weight gain
- Liver impairment: monitor LFTs
- Fluid retention - therefore contraindicated in heart failure. The risk of fluid retention is increased if the patient also takes insulin
- Recent studies have indicated an increased risk of fractures

NICE guidance on thiazolidinediones

- Only continue if there is a reduction of > 0.5 percentage points in HbA1c in 6 months

Further reading:

Pioglitazone BNF

Question 139

According to the Medicines and Healthcare products Regulatory Agency which of the subsequent drugs used in the management of type 2 diabetes mellitus is associated with an increased risk of pancreatitis?

- **A)** Exenatide
- **B)** Canagliflozin
- **C)** Metformin
- **D)** Pioglitazone
- **E)** Gliclazide

Answer

Correct answer : Exenatide

The Medicines and Healthcare products Regulatory Agency warn that exenatide is associated with an increased risk of severe pancreatitis and renal impairment. Exenatide, the first-in-class incretin mimetic, is a glucagon-like-peptide-1 analogue that stimulates insulin release from pancreatic ß cells in a glucose-dependent manner. If pancreatitis is diagnosed, exenatide should be permanently discontinued. Exenatide is also not recommended for use in patients with end-stage renal disease or severe renal impairment.

Exenatide and pancreatitis

Question 140

Which of the drugs listed, used in the management of diabetes mellitus, is most likely to be associated with cholestasis?

- **A)** Acarbose
- **B)** Dapagliflozin
- **C)** Gliclazide
- **D)** Metformin
- **E)** Pioglitazone

Answer

Correct answer : Gliclazide

Drug-induced liver disease is generally divided into hepatocellular, cholestatic or mixed. There is however considerable overlap, with some drugs causing a range of changes to the liver. Sulphonylureas may cause hepatobiliary disorders, with raised hepatic enzymes, hepatitis, and cholestatic jaundice. Gliclazide should be discontinued if this occurs. It usually disappears rapidly after discontinuation of drug.

Question 141

A 59 year old female with a two year history of type 2 diabetes presents for her annual review. She takes metformin 1g bd and also glicalzide 160mg bd. Her weight has declined over the last year, with a weight of 70kg and a BMI of 23.2 kg/m^2. She also complains of some thirst and finds that she needs to get up two to three times per night to pass urine. Her HbA1c is 9.2% (80 mmol/mol) and one year ago it was 7.5% (60 mmol/mol). Which of the following would be the most appropriate approach to managing this woman's diabetes?

- **A)** Add a DPP-IV inhibitor
- **B)** Add a GLP-1 analogue
- **C)** Add pioglitazone
- **D)** Commence insulin
- **E)** Increase dose of metformin and gliclazide

Answer

Correct answer : Commence insulin

Despite this patient being on maximal dual oral hypoglycaemic agents her glycaemic control is poor and she has lost weight. Together with the persisting osmotic symptoms, this would suggest that the patient is becoming insulin deficient and so insulin would be the most logical treatment in this case and, supported by current NICE guidance.

Question 142

A 31 year old male attends clinic complaining of weight loss, tiredness and thirst. He has encountered these problems over the last 3 months and has lost approximately 7kg over this time. There is no family history of any medical conditions of note. He does not take any medications, drinks little and his weight is 74kg with a BMI of 22.8kg/m^2.
His results reveal a plasma glucose of 18.8 mmol/l (3.5-5.5) and his HbA1c is 11.8% (105 mmol/mol) (<6). Which of the following would be the most appropriate initial approach to managing this patient's diabetes?

- **A)** Commence Liraglutide
- **B)** Commence gliclazide
- **C)** Commence insulin
- **D)** Commence metformin
- **E)** Lifestyle intervention only initially with consideration of drugs after this approach

Answer

Correct answer : Commence insulin

This young man has lost weight, has a normal BMI and presents with osmotic symptoms. This together with the high glucose suggests a diagnosis of type 1 diabetes and the patient should be commenced on insulin as the initial therapy. Further investigation would be expected to reveal positive autoantibodies to islet cell or Glutamic Acid Decarboxylase (GAD) both being markers of autoimmune pancreatice beta cell destruction.

Question 143

A 72 year old male has a ten year history of type 2 diabetes and is receiving treatment with glicalzide 160mg bd as well as metformin 1g bd. His most recent HbA1c is 8.8% which has deteriorated over the last year from 7.6%. His weight is 103kg and his BMI is 33.6kg/m^2. Which of the following would be the most appropriate approach to managing this patient?

- **A)** Add canagliflozin
- **B)** Add orlistat
- **C)** Add sitagliptin
- **D)** Commence insulin
- **E)** Continue treatment unchanged

Answer

Correct answer : Add canagliflozin

This patient’s glycaemic control has deteriorated over the last year or so as reflected by a sub-optimal HbA1c despite optimal dual oral hypoglycaemic agents. Thus the most appropriate approach would be the addition of an SGLT-2 inhibitor which offers significant reduction in CV risk as revealed by studies such as EMPA-REG in preference to a DPP-IV inhibitor. Greater reductions in HbA1c could be expected too.

NICE Guidelines

Question 144

A 55 year old man is commenced on treatment with simvastatin 40 mg daily. His BMI is 30 kg/m2 and his BP IS 130/90 mm hg. Which of the following risks is deemed to increase with the use of statin therapy?

- **A)** Diabetes mellitus
- **B)** Erectile dysfunction
- **C)** Immune hypoadrenalism
- **D)** Ischaemic heart disease
- **E)** Multiple sclerosis

Answer

Correct answer : Diabetes mellitus

Statins have been shown through meta-analyses to be associated with a 23% increased risk of new onset diabetes and the FDA warned of this phenomenon in 2012 following results of the JUPITER study. However, statins are without question drugs that reduce CV risk and appear to offer beneficial effects in ED.

Journal of Pharmacotherapy and pharmacotherapeutics (2014)Statin induced diabetes and its clinical implications

Question 145

A 55 year old man with type 2 diabetes is being treated with metformin and gliclazide. His HbA1c is 76 mmol/mol (9.1%). It is decided to commence him on empagliflozin.
Which of the following describe this class of drug?

- **A)** Dipeptidyl peptidase –IV inhibitor
- **B)** Glucagon-like peptide agonist
- **C)** Potassium channel inhibitor
- **D)** Sodium glucose co-transporter-1 inhibitor
- **E)** Sodium glucose co-transporter-2 inhibitor

Answer

Correct answer : Sodium glucose co-transporter-2 inhibitor

Empagliflozin like canagliflozin and dapagliflozin is a SGLT-2 inhibitor which prevents the reabsorption of glucose from the proximal tubule of the nephron. Consequently it increases renal losses of glucose and the class of agents pose an exciting development in the treatment of diabetes.

Medline Plus (2016) Empagliflozin

Question 146

Empagliflozin was used in the landmark EMPA-REG study as an adjunctive treatment to standard care in subjects with type 2 diabetes. Which of the following were the reported results of EMPA-REG?

- **A)** No change in HbA1c but reduced progression of nephropathy
- **B)** Reduced cardiovascular events and all-cause mortality
- **C)** Reduced HbA1c with reductions in all microvascular complications
- **D)** Reduced HbA1c yet increased risk of major acute cardiovascular event (MACE)
- **E)** Reduced microvascular complications but unchanged all-cause mortality

Answer

Correct answer : Reduced cardiovascular events and all-cause mortality

EMPA-REG was an outcome study in over 7000 type 2 subjects treated with empagliflozin plus standard care versus standard care. The primary outcome measure was death from cardiovascular causes, nonfatal myocardial infarction or nonfatal stroke and was reduced from 12.1% to 10.5%. Roughly 25% reduction in the composite end-point. Death from any causes fell from 8.3% to 5.7%

The New England Journal of Medicine, Zinman B et al (2015) Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes

Question 147

A 50-year-old man with poorly controlled type 2 diabetes presents to the follow up annual diabetes clinic. He has had vomiting and abdominal bloating for a few months. He denies any weight loss or diarrhoea .He has a past medical history of hypertension, ischaemic heart disease and gastroesophageal reflux. His diabetes related complications are retinopathy and nephropathy. He is a smoker with a 20-pack year history. He is taking, lansoprazole, aspirin, ramipril, atenolol and simvastatin.

On examination, he has central obesity and his general and systemic examination are unremarkable. About 6 months ago his HbA1C was 101 mmol/L. He undergoes gastric motility testing which shows gastroparesis. Which of the following antiemetics has the strongest evidence for effectiveness for this condition?

- **A)** Cyclizine
- **B)** Domperidone
- **C)** Erythromycin
- **D)** Metoclopramide
- **E)** Omeprazole

Answer

Correct answer : Domperidone

Explanation:

For adults with type 2 diabetes who have vomiting caused by gastroparesis, there is not strong evidence that any available antiemetic therapy is effective. Yet some people do benefit from domperidone, erythromycin or metoclopramide. The strongest evidence for effectiveness is for domperidone, but prescribers must take into account its safety profile, in particular its cardiac risk and potential interactions with other medicines.

Reference:

1. NICE Guidance (2017), Type 2 diabetes in adults: management, National Institute for Health and Care Excellence

Question 148

A 45-year-old male of Afro-Caribbean origin presents with a 5-day history of feeling unwell with polyuria and nocturia. He had a past history of hypertension for which he was being treated with losartan and atorvastatin. He was also taking pantoprazole for reflux.

On examination, the clinician felt he could smell ketones. He had a BMI of 33kg/m^2, had a pulse of 100 bpm reg, seemed dehydrated and had a blood pressure of 108/76 mmHg, with a respiratory rate of 22/min.

Investigations of relevance revealed:

Test	Result	Normal Range
Urea	12.3 mmol/l	(3-8)
Creatinine	160 micromol/l	(50-100)
Glucose	19.9 mmol/l	(3.5-5.5)
HbA1c	10.9% or 96 mmol/mol	
pH	7.27	
Blood ketones	4.1 mmol/l	(<0.6)

He was treated as per diabetic ketoacidosis with IV insulin and fluid resuscitation. Further investigations returned to reveal the following results:

Anti-GAD antibody	Negative
Anti-Islet Cell Ab	Negative
Fasting C-peptide	350 pmol/l (170-900)

After resolution of his DKA, he was started on a basal-bolus insulin regimen with titration of the dose to insulin glargine 48 iu and insulin aspart 20 iu with meals achieving glucose of around 8-12 mmol/l.

Which of the following is the likely diagnosis in this patient’s case?

- **A)** Diabetes prone ketoacidosis
- **B)** Latent-onset diabetes of adulthood (LADA)
- **C)** Maturity-onset diabetes of youth (MODY)

- **D)** Type 1 diabetes
- **E)** Type 2 diabetes

Answer

Correct answer : Diabetes prone ketoacidosis

Explanation:

This middle-aged man of Afro-Caribbean origin is obese and presents with DKA. One would therefore think that the diagnosis is most likely type 1 diabetes or LADA. However, the beta-cell antibodies are negative and, in fact, the c-peptide is normal indicating an adequate islet cell reserve. Therefore, the diagnosis to consider here is that of diabetes-prone ketoacidosis sometimes described as type 1.5 diabetes. In this case, the patient may not require insulin for ongoing management and could be treated with oral or injectable agents such as GLP-1 analogues.

KPD has been classified also with the A (antibody presence + or -) B (beta-cell function + or -) classification. In this case, with absent antibodies A- and good beta-cell function (B+) (as suggested by the C-peptide), he'd be classified as A-B+ very suitable for agents other than insulin.

Reference:

- Balasubramanyam, A., Nalini, R., Hampe, C.S. and Maldonado, M., 2008. Syndromes of ketosis-prone diabetes mellitus. Endocrine reviews, 29(3), pp.292-302.

Question 149

A 20-year-old university student returns to diabetes follow up clinic with osmotic symptoms. He had been diagnosed with type 1 diabetes about 8 years ago. His home blood glucose readings are in the teens. His last HbA1c 3 months ago was 88 mmol/mol (10.2%). He has been treated with multiple daily injection therapy (MDI) and he tests blood sugars 4 to 5 times a day. His past medical history includes hypothyroidism for which he takes thyroxine. He is a smoker of 10 cigarettes a day. He is fed up with his suboptimal control of diabetes and he is enquiring about insulin pump therapy. According to the NICE guidelines (TA 151) what level of HbA1c is considered suitable for insulin pump therapy?

- **A)** 64 mmol/L (8%)
- **B)** 69 mmol/L (8.5%)
- **C)** 75 mmol/L (9%)
- **D)** 84 mmol/L (9.8%)
- **E)** 95 mmol/L (10.8%)

Answer

Correct answer : 69 mmol/L (8.5%)

Explanation:

Continuous subcutaneous insulin infusion (CSII or 'insulin pump') therapy is recommended as a treatment option for adults and children 12 years and older with type 1 diabetes mellitus provided that attempts to achieve target haemoglobin A1c (HbA1c) levels with multiple daily injections (MDIs) result in the person experiencing disabling hypoglycaemia.

Disabling hypoglycaemia is defined as the repeated and unpredictable occurrence of hypoglycaemia that results in persistent anxiety about recurrence and is associated with a significant adverse effect on quality of life

or

HbA1c levels have remained high (that is, at 8.5% [69 mmol/mol] or above) on MDI therapy (including, if appropriate, the use of long-acting insulin analogues) despite a high level of care.

Question 150

As per the NICE [NG3] guidelines on diabetes in pregnancy, which of the following criteria makes the diagnosis of gestational diabetes?

- **A)** 1 hour postprandial plasma glucose (PPG) of 7.8 mmol/L or above
- **B)** 2 hour postprandial plasma glucose (PPG) of 7.8 mmol/L or above
- **C)** Fasting plasma glucose (FPG) of 5.4 mmol/L or above
- **D)** Fasting plasma glucose (FPG) of 8 Mmol/L or more
- **E)** Fasting plasma glucose (FPG) of 6 mmol/L or above

Answer

Correct answer : 2 hour postprandial plasma glucose (PPG) of 7.8 mmol/L or above

Explanation:

As per the NICE guidelines 2015, diagnose gestational diabetes if the woman has either:

- A fasting plasma glucose level of 5.6 mmol/litre or above or
- A 2-hour plasma glucose level of 7.8 mmol/litre or above

Reference:

NICE Guidance (2015), Diabetes in pregnancy: management from preconception to the postnatal period, National Institute of Health and Care Excellence

Question 151

A 60-year-old man was diagnosed with type 1 diabetes at the age of 5. He has had poor control for the last 10 years. He was admitted with a stroke and commenced enteral feeding, which was titrated up to the full rate over 48 hours. He was given an intravenous insulin infusion – a variable rate intravenous insulin infusion (VRIII) for the first 72 hours of his hospital admission, with hourly capillary glucose (CBG) monitoring. Later VRIII was converted to subcutaneous premixed insulin at 0 and 6 hours of enteral feeding. Feed was stopped to give medication. The ward nurse noticed that the patient was confused but alert and his capillary blood glucose was 3.2 mmol/L. The patient had no intravenous access. What is the next appropriate step to treat hypoglycaemia as per the Joint British Diabetes Societies (JBDS) guidelines?

- **A)** 110mls of Fortisip via NG tube
- **B)** 300mls of 10 % dextrose stat
- **C)** 50mls of 50% of dextrose stat
- **D)** Glucagon 2 mg intravenously
- **E)** Restart feed rapidly to deliver 15 to 20 grams of carbohydrate

Answer

Correct answer : Restart feed rapidly to deliver 15 to 20 grams of carbohydrate

Explanation:

As per the JBDS guidelines, if a patient has blood glucose levels less than 4 mmol/l give one of the following treatments (if the patient has no IV access give via nasogastric tube (NGT) ONE of the following):

- 2 Glucogel tubes - not for use with fine bore NGT
- Lucozade – 100 ml (Lucozade Energy Orange) or fruit juice to provide 15-20 g carbohydrate
- 110 – 140 ml Fortitude® (NOT Fortisip®) to give 15-20 carbohydrate
- Re-start feed to rapidly deliver 15 – 20 g carbohydrate

Follow these treatments by FLUSHING THE NGT WITH WATER.

Alternatively: Give IM Glucagon injection (providing no severe hepatic disease or Repeated hypos)

Reference:

1. Joint British Diabetes Societies (JBDS) for inpatient care, (2012),Glycaemic management during the inpatient enteral feeding of stroke patients with diabetes, NHS Diabetes

Question 152

A 60-year-old man was diagnosed with type 2 diabetes at the age of 40 and has had poor blood sugar control for the last few years. He has been taking metformin for his diabetes. He has not previously been on insulin. He was recently admitted with a stroke and commenced on enteral feeding, which has been titrated up to the full rate over a period of 48 hours. His blood sugars are persistently above 12 mmol/L despite metformin suspension powder via enteral feeding. The team looking after the patient has requested advice from the diabetes team. The diabetes team has decided to initiate subcutaneous premixed insulin to be given at the start and midpoint of enteral feed. What total dose of insulin does this patient require in 24 hours as per the Joint British Diabetes Societies (JBDS) guidelines?

The patient's weight is 68 kg

Carbohydrate content of feed (g/100 ml) = 12.3

Intended infusion rate of enteral feed (ml/hour) = 75

Intended duration of feed (hrs. per day) = 20

- **A)** 12 units
- **B)** 18.5 units
- **C)** 20 units
- **D)** 30 units
- **E)** 40 units

Answer

Correct answer : 18.5 units

Explanation:

This is a Type 2 diabetes patient weighing 68 kg who was not previously on insulin.

Carbohydrate content of feed (g/100 ml) = 12.3

Intended infusion rate of enteral feed (ml/hour) = 75

Intended duration of feed (hrs. per day) = 20

Not previously on insulin - therefore insulin carbohydrate ratio 1: 10

$$\text{Total Humulin M3 dose} = \frac{12.3 \times 75 \times 20}{10 \times 100} = 18.45 \text{ units/24 hrs}$$

Step 1: Total carbohydrate intake from enteral feed

That is the total carbohydrate intake expected from the enteral feed over the duration of the feed.

This is calculated as:

[Infusion rate (ml/hour)] x [carbohydrate content (g/100 ml)] x [duration of feeding] ÷100

Step 2 Carbohydrate-to-insulin ratio (CIR)

This is how many grams of carbohydrate/glucose are covered by 1 unit of insulin. The blood glucose rise from enteral feeds is much more than would occur for normal meals, therefore, 1 unit of insulin will cover less of a carbohydrate load.

i. If the **patient is not usually on insulin** use a CIR value of 10.
ii. If the usual **Total Daily Insulin Dose (TDID)** is less than 40 units use a value of **8**.
iii. If the usual **Total Daily Insulin Dose (TDID)** is more than 40 units use a value of **6**.

Step 3. Daily nutritional insulin requirement

This is the daily insulin required to cover the enteral feed over the duration of feeding (e.g. 16, 20, 24 hrs). This is calculated as:

[Total carbohydrate intake from feed] **divided by** [Carbohydrate-to-insulin ratio]

This number of units is then divided into two doses: the first to be given at the start of the feed and the other given at the midpoint of the feed.

Joint British Diabetes Societies (JBDS) for inpatient care, (2012),Glycaemic management

during the inpatient enteral feeding of stroke patients with diabetes, NHS Diabetes

Question 153

A 43-year-old woman is admitted for elective cholecystectomy. She has a 12-year history of type 2 diabetes mellitus controlled with metformin 850 mg three times daily and gliclazide 160 mg twice daily.

On the first postoperative day, she feels sick and refuses breakfast. However, she has been given her usual medication. Three hours later, she is found drowsy and confused in her bed, and is unable to cooperate with the nurses. Her capillary blood glucose concentration is 2.8 mmol/L. An assessment shows that it is safe for her to swallow. According to the Joint British Diabetes Societies (JBDS) guidelines for the management of inpatient hypoglycaemia, what is the most appropriate action to take as a result of this finding?

- **A)** Glucagon 2 mg intramuscularly
- **B)** Glucose 20% 200 mL intravenously over 10 min
- **C)** Orange juice 50 mL
- **D)** Two biscuits followed by milk 250 mL
- **E)** Two tubes of glucose 40% gel orally

Answer

Correct answer : Two tubes of glucose 40% gel orally

Explanation:

As per the JBDS guidelines on inpatient hypoglycaemia management:

- For adults who are conscious, orientated and able to swallow, give 15-20 g quick acting carbohydrate of the patient's choice where possible.
- Some examples are: 150-200 ml pure fruit juice e.g. orange or 90-120 ml of original Lucozade®.
- (Preferable in renal patients) or 5-7 Dextrosol® tablets (or 4-5 Glucotabs®)or 3-4 heaped teaspoons of sugar dissolved in water.
- Repeat the capillary blood glucose measurement 10-15 minutes later. If it is still less than 4.0 mmol/L, repeat treatment for up to 3 cycles. If blood glucose remains less than 4.0 mmol/L after 45 minutes or 3 cycles, contact a doctor.

Joint British Diabetes Societies (JBDS) for inpatient care, (2012),Glycaemic management during the inpatient enteral feeding of stroke patients with diabetes, NHS Diabetes

Question 154

A 29-year-old woman is referred to clinic after she had been found to have a random plasma glucose concentration of 11.5 mmol/L. She has no symptoms, appears well and has no complications.

During an elective admission for a tonsillectomy at the age of 12, it had been noted that she had mildly raised plasma glucose. She had gestational diabetes during her last pregnancy about 3 years ago during which she had required treatment with insulin from 33 weeks' gestation. Insulin was stopped after delivery. She was adopted and has lost contact with the family but she heard that her father had diabetes. On examination, her body mass index is 33 kg/m2. She undergoes an oral glucose tolerance test (75 grams) and her results are:

		Normal Ranges
Fasting plasma glucose	7.6 mmol/L	(3.0-6.0)
2-hour plasma glucose	10.8 mmol/L	(<7.8)

What is the most likely cause of her diabetes?

- **A)** GCK mutation
- **B)** HNF-1ß mutation
- **C)** Latent autoimmune diabetes of adults
- **D)** Mitochondrial diabetes
- **E)** Type 2 diabetes mellitus

Answer

Correct answer : GCK mutation

Explanation:

This patient has maturity onset diabetes of the young (MODY) which is likely due to a glucokinase gene (GCK) mutation. MODY is an autosomal dominant disorder and accounts for 0.5 % to 1% of diabetes.

A MODY patient has the following characteristics:

- Young age of onset (under 45 years)
- Absence of autoimmune markers
- Absence of insulin resistance
- C-peptide positive even after treatment with insulin

The majority of MODY cases are due to heterozygous mutations in genes encoding for the enzyme glucokinase and hepatocyte nuclear factors (HNF1A, HNF4A and HNF1B)

Individuals with GCK - MODY mutations are often asymptomatic. GCK - MODY individuals can have mild hyperglycaemia even many years after initial diagnosis with no microvascular complications observed. In contrast, individuals with HNF mutations may require insulin therapy and develop microvascular complications.

Thanabalasingham, G. and Owen, K.R., 2011. Diagnosis and management of maturity onset diabetes of the young (MODY). BMJ, 343(7828), pp.837-42.

Question 155

A 40-year-old man of Afro-Caribbean descent was reviewed in the diabetes clinic. About 6 months ago, he had been diagnosed with type 2 diabetes mellitus. He had been asymptomatic and had no family history of cardiovascular disease but was a smoker.

On examination, his blood pressure was consistently over 150/92 mmHg despite lifestyle interventions, his weight was 90 kg and his body mass index was 32 kg/m^2. His serum creatinine was normal and there was no microalbuminuria on urine analysis.

According to the NICE (NG 28) guidelines for the management of type 2 diabetes, what is the most appropriate step?

- **A)** Observe and repeat blood pressure in 2 weeks
- **B)** Start ACE inhibitor
- **C)** Start beta-blocker
- **D)** Start calcium antagonist
- **E)** Start thiazide diuretic

Answer

Correct answer : Start ACE inhibitor

Explanation:

The first-line antihypertensive drug treatment for a person of African or Caribbean family origin should be an ACE inhibitor with an escalation to either a diuretic or a generic calcium-channel blocker.

Reference:

Type 2 diabetes in adults: management

Question 156

A 35-year-old man with a 20 year history of type 1 diabetes (HbA1C of 85 mmol) had been having recurrent unexplained hypoglycemic episodes. Real time continuous glucose monitoring (CGM) is considered in this patient to address the glycemic issues. As per the NICE guidelines for type 1 diabetes in adults: diagnosis and management (NG17), which of the following features would make him suitable for CGM?

- **A)** Extreme fear of hypoglycemia
- **B)** Frequent asymptomatic hypoglycemia (more than 2 episodes per week) and not interfering with activities
- **C)** Hyperglycemia (HBA1C>75mmol) despite testing more than 6 times a day
- **D)** HbA1c above 75 mmol/mol
- **E)** More than one episode of severe hypoglycemia in a year with obvious precipitating cause.

Answer

Correct answer : Extreme fear of hypoglycemia

Explanation:

The NICE guidelines (NG 17) recommend real time continuous glucose monitoring (CGM) in following group of patients. They should be willing to commit to using it at least 70 % of the time and to calibrate it as needed and who have ANY of the following despite optimised use of insulin therapy and conventional blood glucose monitoring:

1. More than 1 episode a year of severe hypoglycaemia without an obvious precipitating cause
2. Frequent asymptomatic hypoglycaemia (>2 episodes per week) and interfering with daily activities
3. Extreme fear of hypoglycaemia
4. hyperglycaemia (>75mmol) despite testing more than 10 times a day, Continue CGM only if HBA1C can be sustained at or below 53mmol and there has been fall in HBA1C of 27mmol or more.

Reference:

Type 1 diabetes in adults: diagnosis and management

Question 157

A 12-year-old girl of European descent had been reviewed in the diabetes clinic. She had been diagnosed with type 1 diabetes at the age of 5. She was on a basal bolus regime. She always had good glycaemic control, but recently it had deteriorated with a HBA1C of 85mmol/mol. She has had 2 episodes of diabetic ketoacidosis in the last year. Which of the following hormones is most likely to be responsible for the deterioration in glycaemic control?

- **A)** Cortisol
- **B)** Growth hormone
- **C)** Oestrogen
- **D)** Progesterone
- **E)** Thyroxine

Answer

Correct answer : Growth hormone

Explanation:

Glycaemic control worsens during puberty as the lean body mass doubles, which increases insulin requirements. There is an increase in insulin resistance during puberty. These behavioural changes and psychosocial issues occurring during adolescence further worsen glycaemic control. The excessive GH release during puberty in subjects with IDDM might lead to insulin resistance. Bioavailability of IGF1 is decreased and this increases GH secretion, thus causing insulin resistance. Excessive GH secretion in type 1 diabetes during puberty also has significant effects on ketogenesis resulting in diabetic ketoacidosis.

Question 158

A 57-year-old woman is admitted with fever, malaise and soreness of the left leg. The foreleg has become increasingly red and painful over the last 24 hours. She is a type 2 diabetic and is well controlled on metformin and sitagliptin. She also takes ramipril and simvastatin. She describes being penicillin allergic, having had a rash when she had ampicillin in her youth. On examination she has a temperature of 38.9C, a pulse of 110 bpm and a blood pressure of 118/60 mmHg. She has an erythematous swelling of the left leg extending from the foot to the knee. Blood results reveal:

Test	Result	Normal range
White cell count	12.1x109/l	3-10
CRP	180 mg/l	<5
U+Es	Normal	
Glucose	15.5 mmol/l	

Which of the following is the most appropriate treatment for this patient?

- **A)** Admit and commence IV clarithromycin
- **B)** Admit and commence IV co-trimoxazole
- **C)** Admit and commence IV flucloxacillin
- **D)** Discharge on oral doxycycline
- **E)** Discharge on oral flucloxacillin

Answer

Correct answer : Admit and commence IV clarithromycin

There are 2 considerations here. Firstly the question of whether to admit or not. The Eron class would suggest that the patient needs to be admitted; she is systemically unwell with tachycardia and pyrexia, and is also diabetic, so she would be classified as Eron class 3. Now it comes down to which treatment to select. This patient is penicillin allergic so a beta lactam should not be used. The alternatives recommended for penicillin allergic patients are either IV clarithromycin or IV clindamycin.

References:

- NICE Clinical Knowledge Summaries (CKS), 2015. Cellulitis - acute: Diagnosis.
- Clinical Resource Efficiency Support Team (CREST), 2005. Guidelines on the management of cellulitis in adults.

Question 159

A 64-year-old man with a 28-year history of type 2 diabetes mellitus has had deterioration in renal function recently. He attended the renal clinic for consideration of maintenance haemodialysis. He always had poor glycaemic control. His HbA1c 2 months ago was 78 mmol/mol (9.3%). His past medical history includes ischaemic heart disease, diabetic retinopathy and diabetic neuropathy. He was an ex smoker. He refused to be started on insulin due to needle phobia. He was treated with gliclazide, linagliptin and pioglitazone for his diabetes.
Investigations:

		Normal Ranges
Creatinine	480 µmol/L	(60–110)
Urine micro albumin/ creatinine	70 mcg/mg	(<2.5mcg>

Which of the following is an anti-diabetic medication that can be used in a maintenance haemodialysis patient?

- **A)** Alogliptin
- **B)** Dapagliflozin
- **C)** Gliclazide
- **D)** Metformin
- **E)** Pioglitazone

Answer

Correct answer : Alogliptin

Explanation:

Sulfonylureas are not licensed for use in patients on maintenance hemodialysis and should be avoided because of the high incidence of hypoglycaemia.

Linagliptin, sitagliptin, vildagliptin and alogliptin can be used but dose reductions for sitagliptin, vildagliptin and alogliptin are required.

No dose adjustment is needed for pioglitazone for impaired renal function but it is not licensed for use in patients with maintenance hemodialysis.

Repaglinide can be considered in the hemodialysis patient. Dose reductions are to be expected and it should be noted that experience in this group is limited therefore increased monitoring is required.

Reference:

- Management of adults with diabetes on the haemodialysis unit,, Joint British Diabetes Societies for Inpatient Care (JBDS)

Question 160

A 65-year-old man with poorly controlled type 2 diabetes mellitus attended orthopaedic clinic for severe left knee pain at rest. He had been diagnosed with osteoarthritis and the surgeon recommended a knee replacement. However, his surgery is delayed due to poor glycaemic control (HbA1C was 101 mmol/L (11.4%)). The surgeon had referred the patient to the diabetes clinic to optimise his glycaemic control.

As per the JBDS guidelines in the management of adults with diabetes undergoing surgery and elective procedures, what level of Hba1c is considered safe to proceed with an elective surgery?

- **A)** 69 mmol/mol (8.5%)
- **B)** 73 mmol/mol (8.8%)
- **C)** 79 mmol/mol (9.4%)
- **D)** 81 mmol/mol (9.6%)
- **E)** 85 mmol/mol (9.9%)

Answer

Correct answer : 69 mmol/mol (8.5%)

Explanation:

The team responsible for the patient's' usual, ongoing diabetes care – i.e. primary or secondary care – should aim to optimise glycaemic control (a HbA1c of less than 69 mmol/mol (8.5%)) prior to their surgical referral and it is felt that further optimisation is safely achievable. They should be able to postpone any elective procedure to facilitate this optimisation.

Reference:

- Dhatariya, K., Flanagan, D., Hilton, L., Kilvert, A., Levy, N., Rayman, G. and Watson, B., 2011. Management of adults with diabetes undergoing surgery and elective procedures: improving standards. NHS, UK, April

Question 161

A 68-year-old man with poorly controlled type 2 diabetes mellitus was admitted for elective knee replacement, which was planned for the next day. His past medical history includes hypertension and hypercholesterolaemia. He had been taking premixed human insulin for his diabetes. His latest HbA1C one month ago was 68 mmol/mol (8.4%). His blood pressure and cholesterol were well controlled with tablets. During this admission his blood glucose were persistently above 12 mmol/L. He expected to miss more than one meal and the team had decided to treat him with a variable rate intravenous insulin infusion (VRIII) to control his blood glucose level.

As per the JBDS guidelines in the management of adults with diabetes undergoing surgery and elective procedures, what is the recommended first choice substrate solution for a VRIII?

- **A)** 0.45 % sodium chloride and KCl
- **B)** 0.9% sodium chloride
- **C)** 0.9% sodium chloride and KCl
- **D)** 5% dextrose in 0.45% sodium chloride and KCl
- **E)** 5% dextrose in 0.9% sodium chloride and KCl

Answer

Correct answer : 5% dextrose in 0.45% sodium chloride and KCl

Explanation:

Patients expected to miss more than one meal should have a VRIII. However, patients who manage their type 2 diabetes mellitus on lifestyle alone or on once daily metformin should only start a VRIII if their capillary blood glucose levels are greater than 12 mmol/L on 2 consecutive occasions.

The recommended first choice substrate solution for a VRIII is 5% dextrose in 0.45% sodium chloride and either 0.15% potassium chloride (KCl) or 0.3% KCl.

Reference:

- Dhatariya, K., Flanagan, D., Hilton, L., Kilvert, A., Levy, N., Rayman, G. and Watson, B., 2011. Management of adults with diabetes undergoing surgery and elective procedures: improving standards. NHS, UK, April

Question 162

A 58-year-old bank manager was reviewed in clinic on a follow-up appointment. He was diagnosed with Type 2 DM about 10 years ago. He had a background history of dyslipidemia and chronic stable angina. He was on aspirin, bisoprolol, isosorbide mononitrate, metformin and rosuvastatin therapy. His elder brother was also known to have Type 2 DM and underwent a coronary artery bypass graft (CABG) operation aged 60.

On examination, his body mass index was 36 kg/m^2. General physical and systemic examination was unremarkable.

Investigations:

HbA1c	65 mmol/mol (8.1%)
Urea	5.6 mmol/L (2.5-7.0)
Creatinine	77 umol/L (60-110)
T Cholesterol	4.5 mmol/L or 174.0 mg/dl
Non HDLc	3.0 mmol or 117.0 mg/dl

Which of the following is the most appropriate therapeutic intervention to reduce his cardiovascular risk according to the current evidence base?

- **A)** Allogliptin
- **B)** Glimepiride
- **C)** Insulin
- **D)** Liraglutide
- **E)** Pioglitazone

Answer

Correct answer : Liraglutide

Explanation:

This man has established cardiovascular (CVD) disease and remains at high risk to develop further coronary events. He has morbid obesity as evidenced by his body mass index of 36 kg/m^2. Addition of liraglutide remains the most appropriate next step in his management based on results of the LEADER trial published in June 2016 (apart from optimisation of his blood pressure and lipid levels).

LEADER was a double blind randomised controlled trial in which patients with Type 2 DM who were at high risk of developing cardiovascular disease (or established CVD) were randomised to receive either liraglutide or placebo therapy. The minimum follow-up for the patients was 42 months.

The primary composite outcome for the trial included:

- Death from cardiovascular causes
- Non-fatal myocardial infarction
- Non-fatal stroke

The patients on liraglutide treatment had a lower risk of the primary composite outcome as compared to the placebo group (hazard ratio, 0.87; 95% confidence interval [CI], 0.78 to 0.97; P<0.001 for noninferiority; P=0.01 for superiority). Death from cardiovascular causes occurred in fewer patients in the liraglutide group (219 patients [4.7%]) than in the placebo group (278 [6.0%]) (hazard ratio, 0.78; 95% CI, 0.66 to 0.93; P=0.007).

The frequencies of non-fatal myocardial infarction and non-fatal stroke were lower in the liraglutide group than in the placebo group, although the differences were not significant.

Reference:

- Marso SP et al. Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes. N Engl J Med 2016; 375:311-322.
- The New England Journal of Medicine: Liraglutide and Cardiovascular Outcomes in Type 2 Diabetes

Question 163

The TECOS trial was conducted to compare the effect of sitagliptin on cardiovascular in comparison to a placebo when added to standard care of managing patients with type 2 diabetes. Which one of the following findings can be taken from the TECOS study?

- **A)** Sitagliptin was associated with increased heart failure requiring hospitalisation
- **B)** The mean HbA1c reduction with sitagliptin of 0.4% was maintained throughout the study period
- **C)** The TECOS study was designed to demonstrate the superiority of sitagliptin over a placebo
- **D)** There was a higher rate of pancreatitis in the sitagliptin group but this was not statistically significantly greater in comparison to the placebo
- **E)** There was statistically significant reductions in cardiovascular deaths when using sitagliptin

Answer

Correct answer : There was a higher rate of pancreatitis in the sitagliptin group but this was not statistically significantly greater in comparison to the placebo

Explanation:

All cardiovascular trials are designed to demonstrate non-inferiority. The sitagliptin proved to be non-inferior in comparison to placebo. There was numerically higher cardiovascular death in sitagliptin group though non-significant statistically. Incretin-based therapies are thought to increase risk of pancreatitis. In this study there was no statistical difference but higher number of pancreatitis in sitagliptin treated group. As opposed to alogliptin and saxagliptin there was no increased risk of heart failure with sitagliptin.

Reference:

- Green, J.B., Bethel, M.A., Armstrong, P.W., Buse, J.B., Engel, S.S., Garg, J., Josse, R., Kaufman, K.D., Koglin, J., Korn, S. and Lachin, J.M., 2015. Effect of sitagliptin on cardiovascular outcomes in type 2 diabetes TECOS trial. New England Journal of Medicine, 373(3), pp.232-242.

Question 164

Which of the following studies was designed to analyse cardiovascular outcomes with saxagliptin in the management of type 2 diabetes?

- **A)** CARMELINA
- **B)** DECLARE
- **C)** EXAMINE
- **D)** SAVOR TIMI-53
- **E)** TECOS

Answer

Correct answer : SAVOR TIMI-53

Explanation

The SAVOR TIMI-53 study published in the NEJM in 2013 was a study designed to demonstrate the non-inferiority of the DPP-IV inhibitor, Saxagliptin vs placebo in the treatment of Type 2 diabetics in relation to cardiovascular outcomes. The study revealed that there was an increased risk of hospitalisation associated with heart failure in the treatment arm.

Reference:

- Scirica, B.M., Bhatt, D.L., Braunwald, E., Steg, P.G., Davidson, J., Hirshberg, B., Ohman, P., Frederich, R., Wiviott, S.D., Hoffman, E.B. and Cavender, M.A., 2013. Saxagliptin and cardiovascular outcomes in patients with type 2 diabetes mellitus. New England Journal of Medicine, 369(14), pp.1317-1326.

Question 165

The main outcome with SAVOR-TIMI was that the saxagliptin was non-inferior to the placebo with regards to primary cardiovascular endpoints. Which of the following secondary endpoint was higher with saxagliptin therapy triggering an additional FDA warning to the labelling of the drug?

- **A)** Cardiovascular death
- **B)** Doubling of creatinine
- **C)** Hospitalisation for heart failure
- **D)** Non-fatal myocardial infarction
- **E)** Worsening of retinopathy

Answer

Correct answer : Hospitalisation for heart failure

Explanation:

SAVOR-TIMI 53 was designed to prove non-inferiority of saxagliptin in comparison to a placebo when added to standard of care. The primary composite end points were similar in both groups: hazard ratio 1.00 (95% CI 0.89–1.12) p=0.99.

The hospitalisation for heart failure was numerically higher and marginally missing statistical signal. The FDA issued a recommendation to include this warning highlighting the potential for heart failure. Alogliptin is the other DPP-4 inhibitor (EXAMINE trial) that showed the increased signal for heart failure and hospitalisation.

Reference:

- Scirica, B.M., Bhatt, D.L., Braunwald, E., Steg, P.G., Davidson, J., Hirshberg, B., Ohman, P., Frederich, R., Wiviott, S.D., Hoffman, E.B. and Cavender, M.A., 2013. Saxagliptin and cardiovascular outcomes in patients with type 2 diabetes mellitus. New England Journal of Medicine, 369(14), pp.1317-1326.

Question 166

Linagliptin is the DPP-4 inhibitor which has the licence to be used even in severe renal impairment. The CARMELINA trial was designed to assess which of the following?

- **A)** Cardiovascular and renal outcomes including patients with eGFR < 15 ml/min
- **B)** Cardiovascular and renal outcomes including patients with eGFR > 15 ml/min
- **C)** Cardiovascular and renal outcomes in patients with low cardio-renal risk
- **D)** Primary composite cardiovascular endpoints
- **E)** Primary renal outcomes and assess progression to ESRD requiring dialysis

Answer

Correct answer : Cardiovascular and renal outcomes including patients with eGFR > 15 ml/min

Explanation:

The CArdiovascular safety and Renal Microvascular outcomE study with LINAgliptin (CARMELINA) was designed to assess both cardiovascular and renal outcomes in high risk Type 2 diabetes cohort (history of vascular disease and urine-albumin creatinine ratio [UACR] >200 mg/g), and high renal risk (reduced eGFR and micro or macroalbuminuria). The study drug proved non-inferior to placebo to meet the primary cardiovascular endpoints. It also showed reduced progression of microalbuminuria.

Reference:

- CARMELINA

Question 167

A 28-year-old woman presents to acute medicine with a two-day history of feeling unwell with polyuria. She has a glucose of 22 mmol/l and a pH of 7.2. She is unaware of any specific family history of diabetes of note.

On examination, she is generally well with a BMI of 32 kg/m^2.

What would be the most useful investigation for this patient?

- **A)** Anti-GAD and anti-islet cell antibodies
- **B)** Anti-TTG antibodies
- **C)** Fructosamine
- **D)** HbA1c
- **E)** HNF-1 mutations

Answer

Correct answer : Anti-GAD and anti-islet cell antibodies

Explanation:

The patient presents with diabetic ketoacidosis and the most important investigation would be the demonstration of autoimmunity as reflected by anti-GAD or anti-islet cell antibodies. Autoantibodies would be expected in roughly 80% of individuals with type 1 diabetes and would of course dictate longer-term insulin initiation. HbA1c is not that relevant in this acute setting and adds little to the management. Rarely, MODY can present like this, but this patient does not have anything to suggest this other than the raised BMI and it is relevant that even in obese patients DKA can occur.

Reference:

- Mcquade, H., Ahmad, S. and Stephen, S. (2016). A rare case of diabetic ketoacidosis (DKA) in a patient with genetically confirmed maturity onset diabetes of young (MODY). Presented at Society for Endocrinology BES 2016. Endocrine Abstracts, 44, EP41.
- Saleh, A. (2015). Diagnosis of type 1 diabetes mellitus in adulthood – a case report. Australian Family Physician, 44(4), pp. 233–235.

Question 168

A 30-year-old woman presents to clinic with symptoms of thirst and polyuria. She has a 10-year history of type 1 diabetes and has sub-optimal control as reflected by an HbA1c of 102 mmol/mol (11.5%). She is listed for a laparoscopic cholecystectomy and the surgical team have asked for your opinion with regard to optimising her glycaemic control. She is currently treated with bd mixed insulin yet confesses to being poorly compliant with treatment as she has had gradual weight gain. She also takes a statin and is using amlodipine as an antihypertensive.

On examination, she has a BMI of 34 kg/^{2}, a blood pressure of 122/80 mmHg and has no overt microvascular complications.

What would be the most appropriate approach to her management?

- **A)** Commence liraglutide in conjunction with her current insulin regime
- **B)** Commence metformin in conjunction with her current insulin regime
- **C)** Refer for diabetes psychological assessment
- **D)** Refer for dietetic review
- **E)** Switch to a basal bolus (qds) insulin regime

Answer

Correct answer : Refer for diabetes psychological assessment

Explanation:

This scenario is not uncommon in clinical practice where the patient expresses concern about the issue of weight gain associated with insulin. In this scenario, it is important to improve glycaemic control to ensure better prognosis and reduce the risk of development of microvascular complications. Referral for appropriate psychological diabetes support is evidence based in terms of improving compliance in such patients.

Reference:

- Kalra, S., Jena, B. N. and Yeravdekar, R. (2018). Emotional and psychological needs of people with diabetes. Indian Journal of Endocrinology and Metabolism, 22(5), pp. 696–704.

Question 169

A 26-year-old woman, who is 26 weeks pregnant with her first pregnancy, undergoes an oral glucose tolerance test as screening for possible gestational diabetes. She has a family history of diabetes, with her mother and elder brother having the disorder, and she has a BMI of 31 kg/m^2.

The results of the OGTT are as follows:

0 mins	Glucose 6.2 mmol
2 hrs	Glucose 7.8 mmol/l

What is the most appropriate approach to the management of this patient?

- **A)** Commence metformin therapy
- **B)** Review her capillary blood glucose profile
- **C)** Start a basal bolus insulin regime
- **D)** Start a bd mixed insulin regime
- **E)** Undertake MODY mutational testing

Answer

Correct answer : Review her capillary blood glucose profile

Explanation:

An OGTT is performed in those at risk of gestational diabetes between 24–28 weeks. It's important that candidates are aware of the new criteria for diagnosis of gestational diabetes. This is an interesting scenario with the patient being diagnosed as having gestational diabetes, as reflected by the fasting glucose of 6.2 mmol/l (above 5.6) and confirmed by the post-OGTT glucose of 7.8 mmol/l (7.8 or above). Initially NICE recommends review of the capillary glucose concentrations, ensuring that fasting glucose concentrations are 5.3 mmol/l for fasting and 7.8 mmol/l or below 1 hr after meals or 6.4 mmol/l 2 hrs after meals. In those whom the blood targets are not met with diet and exercise then metformin should be offered (majority).

Reference:

- NICE (2015). New thresholds for diagnosis of diabetes in pregnancy.
- NICE (2015). NICE guideline [NG3]: Diabetes in pregnancy: management from preconception to the postnatal period. 1.2 Gestational diabetes.

Question 170

You see a 40-year-old woman in the MAU after she was found by her mother in the house unrousable. She was noted to be hypoglycaemic by the ambulance staff and responded to glucose. She is now awake and conscious. She is 26 weeks pregnant in her first pregnancy and has a 15-year history of type 1 diabetes. She conceived through IVF. She is treated with a basal bolus insulin regime and has good glycaemic control, with a pre-pregnancy HbA1c of 42 mmol/mol (6%).

Which of the following would be a risk factor for severe hypoglycaemia in pregnancy in type 1 diabetes?

- **A)** Basal bolus insulin regime
- **B)** Impaired hypoglycaemia awareness
- **C)** IVF pregnancy
- **D)** Stable blood glucose levels
- **E)** Twin pregnancy

Answer

Correct answer : Impaired hypoglycaemia awareness

Explanation:

The most serious risk factor for the development of severe, neuroglycopaenic hypoglycaemia in this patient would be impaired hypoglycaemic awareness. This would be a greater risk factor than a basal bolus (qds) insulin regime as it's more about total daily dose rather than frequency. Other contributory factors include duration of diabetes and a pre-pregnancy HbA1c less than <6.5, with severe hypoglycaemia being more problematic in the first trimester.

Reference:

- Evers, I. M., Ter Braak, E. W., De Valk, H. W., et al. (2002). Risk indicators predictive for severe hypoglycemia during the first trimester of type 1 diabetic pregnancy. Diabetes Care, 25(3), pp. 554–559.

Question 171

A 50-year-old man attends clinic wishing to discuss exercising. He has a 6-year history of type 2 diabetes and has a strong family history. He has decided that he wants to make a change to his life and embark on exercise as he saw that a politician has been ‘cured’ of his diabetes by losing weight and exercising. He is obese, with a BMI of 34 kg/m2, and has a HbA1c of 9.8% (84 mmol/mol).

Which of the following parameters is least likely to improve with the adoption of regular exercise?

- **A)** First-phase insulin response
- **B)** HbA1c
- **C)** Insulin sensitivity
- **D)** Testosterone
- **E)** Triglycerides

Answer

Correct answer : First-phase insulin response

Explanation:

Lifestyle interventions are particularly important, but often underutilised, in the management of type 2 diabetes. Moreover, the Look AHEAD study revealed that it is possible to have remission from type 2 diabetes through intensive lifestyle interventions. Benefits include reduction in blood pressure, increased testosterone (roughly 30% of men with T2DM have hypogonadism), improved glycaemic control and lipid profiles. The first-phase insulin response is least likely to benefit as this is lost very early in impaired fasting glucose or early T2DM.

Reference:

- Del Prato, S. and Tiengo, A. (2001). The importance of first-phase insulin secretion: implications for the therapy of type 2 diabetes mellitus. Diabetes/Metabolism Research and Reviews, 17(3), pp. 164–174.

Question 172

A 25-year-old female is admitted to the MAU with a two-day history of feeling unwell and thirsty. She has a 15-year history of type 1 diabetes, for which she takes a basal bolus regime. She has been struggling with control of her diabetes, whereas in her youth her glycaemic control had been pretty good. She informs you that she has lost weight. However, her records reveal that over the last few years she has been seen in the diabetes, ophthalmology and renal clinics with proliferative retinopathy, amenorrhoea and proteinuria.

On examination, she has a BMI of 17.8 kg/m^2, a pulse of 90 bpm, apyrexial, a blood pressure of 120/80 mmHg and a sweet smell to her breath. Investigations confirm diabetic ketoacidosis. Her glucose is 23 mmol/l, pH 7.26 and her HbA1c is 9.0%.

What is the likely diagnosis?

- **A)** Addison's disease
- **B)** Anorexia nervosa
- **C)** Coeliac disease
- **D)** Disordered eating behaviour
- **E)** Lymphocytic hypophysitis with partial hypopituitarism

Answer

Correct answer : Disordered eating behaviour

Explanation:

The history is of decline in glycaemic control over the last few years associated with weight loss in a young T1DM female. Younger females are often concerned about weight gain with insulin therapy and omit doses for weight loss, and associated with this there is disordered eating behaviour rather than anorexia. In conjunction with weight loss and poor glycaemic control, a hypogonadotropic (secondary) hypogonadism would be expected. Addison's would result in improved insulin sensitivity, with increased likelihood for hypoglycaemia and the blood pressure would maybe be lower. There is an increased risk of coeliac disease in people with T1DM but the presentation is rather unusual for this and one might expect features of malabsorption, diarrhoea etc.

Question 173

A 25-year-old professional rugby player attends clinic keen to improve glycaemic control. He has had type 1 diabetes for the last 8 years and has a high level of physical fitness. However, he has rather erratic blood glucose readings and has had problems in one game latterly, having encountered what was a presumed hypoglycaemic episode, which responded to glucose though he had to leave the field of play. His HbA1c is 5.8%.
What is the best approach to the ongoing management of this patient?

- **A)** Advocate a high glycaemic index diet on match day
- **B)** Enquire about the use of anabolic steroids
- **C)** Omit insulin dose on morning of match day
- **D)** Stop insulin and switch to oral hypoglycaemic agents
- **E)** Suggest continuous blood glucose monitoring to assess glucose concentrations and impact of exercise

Answer

Correct answer : Suggest continuous blood glucose monitoring to assess glucose concentrations and impact of exercise

Explanation:

There is an increasing number of professional sportsmen with diabetes and these require detailed advice on how to manage their insulin requirements plus diet in connection with training and match days. In this scenario, CGM provides real-time data on glucose concentrations under various settings. The insulin and nutritional requirements can be tailored based on these recordings. There are a number of CGMs available now for such patients.

Reference:

- Thomas, F., Pretty, C. G., Signal, M. and Chase, J. G. (2015). Accuracy and performance of continuous glucose monitors in athletes. IFAC-PapersOnLine, 48(20), pp. 1–6.

Question 174

A 61-year-old man presents to acute admissions with central chest pain. He has a 6-year history of HIV infection, for which he takes antiretroviral treatment, and has a background of stable angina. He is diagnosed with acute coronary syndrome. He is appropriately treated, but later during his admission someone spots that his admission glucose was 15.5 mmol/l. A couple of days later a fasting glucose is requested, which returns as 13.8 mmol/l. He confirms that he has a family history of diabetes, with both parents having suffered from type 2 diabetes. Which of the following drugs is most likely to have contributed to hyperglycaemia?

- **A)** Atorvastatin
- **B)** Ramipril
- **C)** Ritonavir
- **D)** Tenofovir
- **E)** Ticagrelor

Answer

Correct answer : Ritonavir

Explanation:

Highly active antiretroviral therapy (HAART) is effective in the treatment of HIV, yet the protease inhibitors such as ritonavir and indinavir are associated with hyperglycaemia through proposed inhibition of the GLUT-4 insulin-regulated transporter. Other side effects related to increased insulin resistance include hypertriglyceridaemia and dyslipidaemia, together with elevated transaminases. Tenofovir is a reverse transcriptase inhibitor. It is not associated with hyperglycaemia.

Reference:

- Dever, L. L., Oruwari, P. A., Figueroa, W. E., et al. (2000). Hyperglycemia associated with protease inhibitors in an urban HIV-infected minority patient population. Annals of Pharmacotherapy, 34(5), pp. 580–584.

Question 175

A 46-year-old man attends clinic complaining of thirst and polydipsia. He has a 5-year background of HIV infection, for which he takes highly active antiretroviral therapy (HAART). He explains that he has a family history of type 2 diabetes, with an elder sister having the disorder. He has put on roughly 3 kg in weight over the last 6–9 months. His fasting glucose is 12.9 mmol/l (3.5–5.5). His HbA1c is 66 mmol/mol (8.2%).

Together with lifestyle advice, what is the most appropriate treatment for this patient?

- **A)** Cannagliflozin
- **B)** Gliclazide
- **C)** Metformin
- **D)** Mixed insulin
- **E)** Sitagliptin

Answer

Correct answer : Metformin

Explanation:

This patient with type 2 diabetes which may have been exacerbated by the protease inhibitors in HAART should be offered lifestyle interventions plus metformin as first-line treatment as per the NICE guidelines.

Reference:

- Avari, P. and Devendra, S. (2017). Human immunodeficiency virus and type 2 diabetes. London Journal of Primary Care, 9(3), pp. 38–42.
- NICE (2015, updated 2019). NICE guideline [NG28]: Type 2 diabetes in adults: management. 1 Recommendations.

Question 176

A 16-year-old male presents to the adolescent clinic with a 3 month history of thirst, frequency of micturition and nocturia. He has a family history of diabetes. Urine analysis revealed glycosuria ++ and haematuria +. Fasting plasma glucose was 9.1 mmol/l. An ultrasound examination of the abdomen was requested which revealed numerous renal cysts.
Which of the following is the likely mode of inheritance for this condition?

- **A)** Autosomal dominant
- **B)** Autosomal recessive
- **C)** Mitochondrial
- **D)** Polygenic
- **E)** X-linked recessive

Answer

Correct answer : Autosomal dominant

Explanation:

The above case describes MODY type 5 due to mutations of HNF-1B, where the patient has early onset diabetes associated with tubule-interstitial disease typified by renal cysts. It is inherited as an autosomal dominant condition.

Reference:

- Orpha (2014) HNF1B-related autosomal dominant tubulointerstitial kidney disease

Question 177

You are reviewing a patient in palliative medicine clinic who has myeloma and is receiving Velcade chemotherapy. He has also been a type 2 diabetic and comments that since commencing the chemotherapy the chronic burning pain in his feet and hands has become worse. He has tried gabapentin for this previously which was tolerated well but of no benefit for the pain.

Which of the following drugs would you consider as most appropriate treatment for his likely diabetic neuropathy?

- **A)** Citalopram
- **B)** Duloxetine
- **C)** Mirtazepine
- **D)** Oxycodone
- **E)** Topical Capsaicin

Answer

Correct answer : Duloxetine

The recent guidance from NICE recommends duloxetine/Gabapentin/Pregabalin or amitriptyline as first line management for diabetic neuropathy. Concurrent use of chemotherapy agents such as Velcade can exacerbate pre-existing neuropathic pains as well as cause new pain.

National Institute for Health and Clinical Excellence.
The pharmacological management of neuropathic pain in adults in non-specialist settings.
https://cks.nice.org.uk/neuropathic-pain-drug-treatment#!scenario

Question 178

A 53-year-old man is diagnosed with type 2 diabetes. He has a family history of diabetes with his father and brother having the disorder. He has a body mass index of 39 kg/m^2. In terms of increased relative rate compared to the background population, to which of the following cancers does obesity most predispose?

- **A)** Colon cancer
- **B)** Kidney cancer
- **C)** Lung cancer
- **D)** Pancreatic cancer
- **E)** Prostate cancer

Answer

Correct answer : Kidney cancer

Explanation

Obesity (BMI above 30) increases risk of cancer in both males and females by the order of 8–10%. The relative increased risk of colon cancer is the order of 1.34, pancreatic cancer 1.19, kidney cancer 1.76 and prostate and lung cancer appears to be neutral. There also appears to be a dose effect with every 1 kg/m^2 increase in BMI above 30. Oesophageal cancer is again far higher than other solid tumours (140% increased). See the studies listed below.

Reference

- Liu, X., Sun, Q., Hou, H., Zhu, K., Wang, Q., Liu, H., Zhang, Q., Ji, L. and Li, D. (2018). The association between BMI and kidney cancer risk: An updated dose-response meta-analysis in accordance with PRISMA guideline. Medicine, 97(44), p. e12860.
- Moghaddam, A.A., Woodward, M. and Huxley, R. (2007). Obesity and risk of colorectal cancer: a meta-analysis of 31 studies with 70,000 events. Cancer Epidemiology and Prevention Biomarkers, 16(12), pp. 2533–2547.
- Parkin, D.M. and Boyd, L. (2011). 8. Cancers attributable to overweight and obesity in the UK in 2010. British Journal of Cancer, 105(2), pp. S34–S37.

Question 179

A 21-year-old girl is a known case of type 1 diabetes since the last 5 years. She is on multi-dose insulin (MDI). Based on her self-monitoring of blood glucose (SMBG) readings, her physician advised her to use an intermittently scanned CGM (isCGM; also called ‘flash’ CGM). Her frequency of glucose measurement using the isCGM has improved. Her glycaemic control has also improved and she is self-managing her insulin doses in a much better way. The patient wants to know more about the data that is derived from the isCGM device called the ambulatory glucose profile (AGP). The patient is an active member of a popular type 1 diabetes internet forum and she has heard about a concept called "Time-in-range" (TIR). TIR is the percentage of the time when the glucose readings from the CGM are between the range of 3.9 mmol/l and 10.0 mmol/l (70 mg/dl and 180 mg/dl). The patient wants to know what TIR value correlates with her target HbA1c which is =53 mmol/mol (7.0%).

- **A)** HbA1c values do not correlate with the Time-in-range values
- **B)** 50-55% of the CGM glucose values in the Time-in-range of 3.9 mmol/l and 10.0 mmol/l (70 mg/dl and 180 mg/dl) correlates with an HbA1c target of =53 mmol/mol (7.0%)
- **C)** 65-70% of the CGM glucose values in the Time-in-range of 3.9 mmol/l and 10.0 mmol/l (70 mg/dl and 180 mg/dl) correlates with an HbA1c target of =53 mmol/mol (7.0%)
- **D)** 70-85% of the CGM glucose values in the Time-in-range of 3.9 mmol/l and 10.0 mmol/l (70 mg/dl and 180 mg/dl) correlates with an HbA1c target of =53 mmol/mol (7.0%)
- **E)** >90% of the CGM glucose values in the Time-in-range of 3.9 mmol/l and 10.0 mmol/l (70 mg/dl and 180 mg/dl) correlates with an HbA1c target of =53 mmol/mol (7.0%)

Answer

Correct answer : 65-70% of the CGM glucose values in the Time-in-range of 3.9 mmol/l and 10.0 mmol/l (70 mg/dl and 180 mg/dl) correlates with an HbA1c target of =53 mmol/mol (7.0%)

Explanation:

Continuous glucose monitoring (CGM) has revolutionised diabetes management and is increasingly being used worldwide by patients and physicians for better management of the glycaemic control in both type 1 and type 2 diabetes patients. One of the more popular forms of CGM is the intermittently scanned CGM (isCGM; also called ‘flash’ CGM) in which the patient applies a sensor to the arm and uses either a reader or a mobile device with a specialized app to ‘read’ the glucose value at that particular point in time. (Murata et al., 2018) The graphical chart derived from the CGM readings is called an Ambulatory glucose profile (AGP). The AGP gives various glycaemic parameters which are useful for both the patient as well as the clinician. One of the more popular parameters derived from the same is the "Time-in-range". TIR is the percentage of the time when the glucose readings from the CGM are between the range of 3.9 mmol/l and 10.0 mmol/l (70 mg/dl and 180 mg/dl). (Advani, 2020) A recent survey conducted amongst patients with diabetes showed that amongst patients with type 1 diabetes and type 2 diabetes on insulin, the TIR is the second most important parameter which has a “Big impact” on the patients’ lives.(Runge et al., 2018)

Several studies have found a correlation between the TIR and the HbA1c value. The TIR of 65-70% correlates with the HbA1c value of =53 mmol/mol (7.0%) which is the target HbA1c in most patients.(Advani, 2020) The recent consensus guidelines on the homogenous use of the data derived from the CGM have advised a TIR of >70% for both type 1 and type 2 diabetes patients.(Danne et al., 2017)

References:

- Advani, A. (2020) ‘Positioning time in range in diabetes management’, Diabetologia, 63(2), pp. 242–252. doi: 10.1007/s00125-019-05027-0.
- Danne, T. et al. (2017) ‘International Consensus on Use of Continuous Glucose Monitoring’, Diabetes Care, 40(12), pp. 1631 LP – 1640. doi: 10.2337/dc17-1600.
- Murata, T. et al. (2018) ‘The Current Intermittent-Scanning CGM Device Situation in Japan: Only Adjunctive Use to SMBG Is Approved and the Latest Health Insurance Coverage Details’, Journal of diabetes science and technology. 2017/12/27. SAGE Publications, 12(3), pp. 729–730. doi: 10.1177/1932296817749860.
- Runge, A. S. et al. (2018) ‘Does Time-in-Range Matter? Perspectives From People With Diabetes on the Success of Current Therapies and the Drivers of Improved Outcomes’, Clinical

diabetes?: a publication of the American Diabetes Association. American Diabetes Association, 36(2), pp. 112–119. doi: 10.2337/cd17-0094.

Question 180

A 55-year-old man attends clinic and is concerned about his weight and risk of developing diabetes. His weight has always been above average, but he has gained more gradually over the last 10 years. He is also concerned as he has a family history of diabetes in that both his elderly parents developed diabetes in middle age.

On examination, he has a BMI of 35 kg/m^2, a waist circumference of 102 cm and a blood pressure of 134/88 mmHg.

You undertake a point-of-care glucose test and his fasting glucose concentration is 5.7 mmol/l (normal range 3.5–5.5).

Which of the following best describes his risk of developing diabetes in the next 5 years?

- **A)** 1%
- **B)** 10%
- **C)** 30%
- **D)** 50%
- **E)** 70%

Answer

Correct answer : 30%

Explanation

This man is obese, has a very high waist circumference and the fasting plasma glucose of 5.7 mmol/l reflects impaired fasting glucose. According to the QDiabetes risk calculator, which is a particularly useful tool to calculate the future risk of developing diabetes, this man's 10-year risk of developing diabetes is 30%. The science underlying this risk calculator was published in the BMJ in 2009 and is listed below. This high risk is also seen in studies such as Diabetes Prevention Programme and Diabetes Prevention Study.

References:

- QDiabetes (2018). QDiabetes diabetes risk calculator.
- Hippesley-Cox, J., Coupland, C., Robson, J., Sheikh, A. and Brindle, P. (2009). Predicting risk of type 2 diabetes in England and Wales: prospective derivation and validation of QDScore. BMJ, 338, b880.

Question 181

A 45-year-old man is evaluated after routine blood tests. His blood work showed a fasting glucose of 116mg/dL (6.4mmol/L). An oral glucose tolerance test (OGTT) with 75 grams of glucose load revealed a 2-hour plasma glucose of 166 mg/dL (9.2mmol/L). He has no medical problems except obesity. His elder sister has diabetes. On examination his pulse is 88/min, blood pressure 130/90mmHg and BMI is 35. Systemic examination shows no abnormalities. His fasting plasma glucose 6 months back was 112 mg/dL (6.2mmol/L).
What is the best treatment for this patient?

- **A)** Intensive lifestyle modification and acarbose
- **B)** Intensive lifestyle modification and metformin
- **C)** Intensive lifestyle modification and rosiglitazone
- **D)** Start basal insulin
- **E)** Start glimepiride

Answer

Correct answer : Intensive lifestyle modification and metformin

Explanation:

This patient has impaired fasting glucose (IFG) defined as a fasting plasma glucose (FPG) level of 100-125mg/dL (5.6-6.9mmol/L) and impaired glucose tolerance (IGT) defined as a 2-hour plasma glucose level of 140-199 mg/dL (7.8-11mmol/L) according to the American diabetes association (ADA). WHO threshold for IFG is 110-125mg/dL (6.1-6.9mmol/L). IFG and IGT are intermediate states between normal glucose regulation and diabetes and are called pre-diabetes. Although this patient does not meet diagnostic criteria for diabetes, intervention is still warranted as both IFG and IGT increase the risk of diabetes and cardiovascular disease. NICE guidelines recommend intensive lifestyle modification. Metformin is recommended for people whose FPG have deteriorated despite an intensive lifestyle change programme or those who are unable to participate, in that if they have a BMI of more than 35. This forms the basis of the NHS diabetes prevention programme (DPP). The ADA consensus statement regarding diabetes prevention states that lifestyle modification and/or metformin should be considered in patients with both IFG and IGT who are younger than 60 years and have a BMI of 35 or greater. Because persons with associated risk factors for diabetes such as a family history of diabetes in first degree relatives or hypertension are more likely to develop diabetes, it is another reason to consider metformin, as in this case.

Although acarbose is effective in delaying the onset of diabetes, its gastrointestinal side effects cannot be tolerated by many patients. So metformin is preferred over the addition of acarbose. Rosiglitazone is as effective as intensive lifestyle modification in delaying or preventing diabetes. However, it is associated with an increased risk of heart failure and myocardial infarction, but not mortality. Therefore, it is not currently recommended for the treatment of prediabetes. Insulin and glimepiride are also not recommended for pre-diabetes.

Reference:

- NICE (2012, updated September 2017) NICE guideline [1PH38]. Type 2 diabetes : prevention in people at high risk
- Hostalec U. et.al. (2015), ‘Therapeutic Use of Metformin in Prediabetes and Diabetes Prevention’ ,Drugs 75:1071-1094

Question 182

A 45-year-old man who has been diabetic for the past 5 years was seen in diabetic clinic. He was initially taking glimepiride 2 mg OD and metformin 1gm BID but his blood sugars were poorly controlled. He started on an insulin basal-bolus regimen as humulin R 8 units before meals and glargine 12 units at bedtime 1 month ago. The patient was concerned about adjustment of insulin bolus dose according to meals. He should be referred to which diabetes education programme?

- **A)** DAFNE
- **B)** X-PERT Diabetes
- **C)** X-PERT Insulin
- **D)** BERTIE
- **E)** DESMOND

Answer

Correct answer : X-PERT Insulin

Explanation:

There are several structured diabetes education courses in the UK. DAFNE course is aimed specifically at people with type 1 diabetes giving them necessary skills to administer the right amount of insulin for the amount of carbohydrates eaten.

X-PERT Diabetes Programme runs in three different formats to cater for people with different types of diabetes as well as those at risk of diabetes. X-PERT prevention of Diabetes is an intensive lifestyle programme aimed at reducing risk of developing type 2 diabetes for people at higher risk. X-PERT Diabetes is for people with type 1 and type 2 diabetes with an emphasis on lifestyle choices. X-PERT insulin is for people with type 1 or 2 diabetes who are treated with insulin.

BERTIE is for anyone with type 1 diabetes who is over the age of 16 years and patients with type 2 diabetes who are treated with MDI (multiple daily injection) involving fast-acting insulin with meals and long-acting insulin. It educates the patients about carbohydrate counting and adjusts insulin doses accordingly. DESMOND is for people with type 2 diabetes that help them to identify their own health risks and to set their own goals.

Question 183

A 52-year-old office worker attends the diabetes clinic for his annual review having been diagnosed 2 years previously. His Hba1c was previously poorly controlled on Metformin 1g bd at 58 mmol/mol (7.5%), but is much better following the addition of sitagliptin and improved diet and exercise 6 months ago and is now 46 mmol/mol (6.4%).

His blood pressure today in clinic was 162/96 mm/Hg having been 151/82 at his last clinic visit. His renal function was normal as was his cholesterol. He is an ex-smoker with a 10 pack year history.

How should his blood pressure be managed?

- **A)** Ace inhibitor
- **B)** Beta blocker
- **C)** Calcium channel antagonist
- **D)** No treatment needed at present
- **E)** Thiazide diuretic

Answer

Correct answer : Ace inhibitor

Explanation:

He has already made efforts with diet and exercise and his blood pressure was sub-optimal at his last clinic visit. Anti-hypertension therapy needs instigating. NICE guidance recommends to reduce clinic blood pressure to below 140/90 mmHg and maintain that level in adults with hypertension aged under 80. NICE also recommends use of an Ace inhibitor as first line in people with type 2 diabetes.

References:

- NICE recommendations hypertension in adults

Question 184

A 52-year-old woman presents with a 2-week history of deteriorating fatigue, nausea, thirst and polyuria. Most recently, she had problems keeping fluids down and the GP had advised admission. She has a 3-year history of type 2 diabetes for which she takes metformin and empagliflozin. Her most recent body mass index is 31. Her glucose as measured in the lab also returns as 8.7 mmol/l and her most recent HbA1c is 7.1%.
Which of the following is the most appropriate approach to the management of this patient?

- **A)** Arrange CT TAP
- **B)** Arrange Covid-19 swab
- **C)** Check blood cultures
- **D)** Check blood ketones and venous gases
- **E)** Check islet cell autoantibodies

Answer

Correct answer : Check blood ketones and venous gases

Explanation:

A diagnosis of euglycaemic diabetic ketoacidosis should be considered in this context, yet the other possibility is that she has LADA. This patient has a rather short history of diabetes and islet cell and GAD auto-antibodies could also be checked, yet the most appropriate investigation here is the ketones and venous gases. In this scenario, it is important to measure capillary ketones to consider/exclude euglycaemic diabetic ketoacidosis (DKA), a potentially life-threatening complication seen with SGLT2 inhibitors.

Reference:

- Plewa MC, Bryant M, King-Thiele R. Euglycemic Diabetic Ketoacidosis. [Updated 2020 Apr 30]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan-.

Question 185

A 22-year-old female with type 1 diabetes attends the clinic and informs you that she intends to become pregnant. She has a 6-year history of type 1 diabetes for which she takes a basal-bolus insulin regimen consisting of NovoRapid and insulin Levemir.

Which of the following is the target HbA1c advocated by NICE that one should aim to be below for pregnancy?

- **A)** 37 mmol/mol (5.5%)
- **B)** 42 mmol/mol (6%)
- **C)** 48 mmol/mol (6.5%)
- **D)** 53 mmol/mol (7%)
- **E)** 58 mmol/mol (7.5%)

Answer

Correct answer : 48 mmol/mol (6.5%)

Explanation:

Tight glycaemic control in those planning pregnancy aiming for an HbA1c at or below 6.5% is advocated by NICE in order to improve fetal and maternal outcomes. This level should also be adopted during the first 12 weeks of pregnancy. The risk of congenital malformations increases in a linear fashion above an HbA1c of 6.3%. Women who have an HbA1c level of 86 mmol/mol (10%) should be advised not to get pregnant because of the associated risks (>14% or 1 in 9 risk of congenital anomaly).

Reference:

- Pregnancy care for women with diabetes. NPID15_Easy_Report_V10.pdf.

Question 186

A woman is seen for her first antenatal appointment. Which of the following would suggest that she needs to be screened for gestational diabetes?

- **A)** A diagnosis of Hashimoto’s disease
- **B)** Age 40 at presentation
- **C)** Asian ethnicity
- **D)** BMI of 27.5 kg/m^2
- **E)** Previous baby weighing 4kg

Answer

Correct answer : Asian ethnicity

Explanation:

The screening factors for gestational diabetes include Black, Asian and Minority Ethnicity (BAME), a sibling or parent with diabetes, a BMI above 30 and previous macrosomia (birthweight above 4.5Kg) or previous pregnancy with gestational diabetes.

Reference:

- Royal College Of Obstetricians & Gynaecologists. Diagnosis and Treatment of Gestational Diabetes Scientific Impact Paper No. 23.

Question 187

A 36-year-old woman has been recently diagnosed with gestational diabetes. This is her first pregnancy. She has been given advice on diagnosis and exercise and has been monitoring her capillary blood glucose concentrations as below.

Day	Fasting	1h after breakfast	1h after lunch	1h after dinner
1	4.8	7.1	6.7	5.9
2	5.3	8.2	7.3	6.2
3	5.1	7.9	6.2	6.2
4	4.7	8.3	7.0	5.9

Which of the following would be the most appropriate approach to the management of this patient?

- **A)** Commence gliclazide 40mg twice daily
- **B)** Commence long-acting insulin at night
- **C)** Commence metformin 500mg once in the morning
- **D)** Commence NovoRapid once before breakfast
- **E)** Commence tds NovoRapid before each meal

Answer

Correct answer : Commence metformin 500mg once in the morning

Explanation:

Targets for fasting levels in gestational diabetes are 5.3 mmol/l with postprandial targets of 7.8 mmol/l or below 1hr and 6.4 mmol/l 2hrs after a meal. In our case, this woman has three readings, 1-hour post-breakfast which are above this threshold. She is only receiving lifestyle interventions, and so she does require treatment to reduce fetal risk. Metformin is regarded as the most appropriate first-line agent in our case and, should this treatment fail to produce adequate glycaemia, then insulin should be initiated.

References:

- Reece, S.W., Parihar, H.S. and LoBello, C., 2014. Metformin in gestational diabetes mellitus. Diabetes spectrum, 27(4), pp.289-295.
- Diabetes in pregnancy: management from preconception to the postnatal period NICE guideline [NG3].

Question 188

A 59-year-old male received a donor renal transplant for an underlying diagnosis of adult polycystic kidney disease. He was otherwise well and had no known past history of diabetes. From the second postoperative day, his fasting glucose concentrations were noted to be 6–9 mmol/L with 2-hour post evening meal glucose of 15–20 mmol/L. He was otherwise well and had made a good recovery from the procedure, eating and drinking normally.
Which of the following is the most appropriate management for this patient?

- **A)** Commence fast acting insulin (tds) with each meal
- **B)** Commence gliclazide 40 mg bd
- **C)** Commence isophane insulin (Humulin I) in the morning
- **D)** Commence metformin 500 mg twice daily
- **E)** No treatment is required at this stage

Answer

Correct answer : Commence isophane insulin (Humulin I) in the morning

Explanation:

Hyperglycaemia post-transplant of solid organs is quite common and requires management, as it represents a risk for graft survival as well as prognosis. PTDM occurs in up to 40% of subjects and may be a consequence of the immunosuppressive therapy as well as other risk factors. The most appropriate approach for this patient would be insulin therapy with intermediate-acting isophane insulin (Humulin I) in the morning, as this will impact most on his marked postprandial excursions.

Reference:

- Chowdhury, T.A., 2019. Post-transplant diabetes mellitus. Clinical Medicine, 19(5), p.392.

Question 189

A 45-year-old male of Afro-Caribbean origin presents with a 5-day history of feeling unwell with polyuria and nocturia. He had a past history of hypertension for which he was being treated with losartan and atorvastatin. He was also taking pantoprazole for reflux.

On examination, the clinician felt he could smell ketones. He had a BMI of 33kg/m^2, had a pulse of 100 bpm reg, seemed dehydrated and had a blood pressure of 108/76 mmHg with a respiratory rate of 22/min.

Investigations of relevance revealed:

Test	Result	Normal Range
Urea	12.3 mmol/l	(3-8)
Creatinine	160 micromol/l	(50-100)
Glucose	19.9 mmol/l	(3.5-5.5)
HbA1c	10.9% or 96 mmol/mol	
pH	7.27	
Blood ketones	4.1 mmol/l	(<0.6)

He was treated as per diabetic ketoacidosis with IV insulin and fluid resuscitation. Further investigations returned to reveal the following results:

Anti-GAD antibody	Negative
Anti-Islet Cell Ab	Negative
Fasting C-peptide	350 pmol/l (170-900)

After the resolution of his DKA, he was started on a basal-bolus insulin regimen.

In clinic 3 months later, he has been titrated to a dose of insulin glargine 48 iu and insulin aspart 20 iu with meals achieving glucose of around 8-12 mmol/l. He has also commenced on metformin 1g bd. His weight has increased 3kg and his HbA1c is now 8.3% (67 mmol/mol).

Which of the following is the most appropriate approach to his ongoing management?

- **A)** Add a GLP-1 analogue and reduce dose of insulin with view to phasing out
- **B)** Add a sulphonylurea and reduce dose of insulin with a view to phasing out

- **C)** Add SGLT-2 inhibitor and reduce dose of insulin with view to phasing out
- **D)** Continue to gradually up titrate his daily insulin dose
- **E)** Switch to twice daily insulin with gradual daily insulin dose escalation

Answer

Correct answer : Add a GLP-1 analogue and reduce dose of insulin with view to phasing out

Explanation:

This middle-aged man of Afro-Caribbean origin is obese and presents with DKA. One would therefore think that the diagnosis is most likely type 1 diabetes or LADA. However, the beta-cell antibodies are negative and, in fact, the c-peptide is normal indicating an adequate islet cell reserve. Therefore, the diagnosis to consider here is that of diabetes-prone ketoacidosis, sometimes described as type 1.5 diabetes. In this case, the patient may not require insulin for ongoing management and could be treated with oral or injectable agents such as GLP-1 analogues.

KPD has been classified also with the A (antibody presence + or -) B (beta-cell function + or -) classification. In this case, with absent antibodies A- and good beta-cell function (B+) (as suggested by the C-peptide), he'd be classified as A-B+ very suitable for agents other than insulin. Consequently, with his increasing weight, he should be considered for a GLP-1 analogue with dose reduction of his insulin with a view to phasing this out entirely.

Reference:

- Balasubramanyam, A., Nalini, R., Hampe, C.S. and Maldonado, M., 2008. Syndromes of ketosis-prone diabetes mellitus. Endocrine reviews, 29(3), pp.292-302.

Question 190

A 50-year-old female was awaiting a cardiac transplant for dilated cardiomyopathy. In her past medical history, she had suffered gestational diabetes. Both her father and elder sister suffer from type 2 diabetes. She has a BMI of 31kg/m^2. An oral glucose tolerance test has revealed a fasting glucose of 5.5 mmol/l with a 2 hr glucose of 9.8 mmol/l.
Which of the following immunosuppressants is most likely to cause post-transplant diabetes mellitus in this patient?

- **A)** Alemtuzumab
- **B)** Azathioprine
- **C)** Ciclosporine
- **D)** Mycophenolate mofetil
- **E)** Tacrolimus

Answer

Correct answer : Tacrolimus

Explanation:

This patient would be expected to have a high risk of developing post-transplant DM as she is obese, had gestational diabetes and has impaired glucose tolerance. Of the immunosuppressive agents listed, tacrolimus, a calcineurin inhibitor (like cyclosporine) is the most diabetogenic of these immunosuppressants. Corticosteroids is an obvious cause and would be rather trite to include in an SCE question.

Reference:

- Chowdhury, T.A., 2019. Post-transplant diabetes mellitus. Clinical Medicine, 19(5), p.392.

Question 191

A 55-year-old man is being considered for solid organ transplantation. He has a fasting glucose of 6 mmol/l and has a BMI of 31kg/m^2.

Which of the following infections is most likely to increase his risk of developing post-transplant diabetes mellitus?

- **A)** Hepatitis A
- **B)** Hepatitis B
- **C)** Hepatitis C
- **D)** Hepatitis D
- **E)** Hepatitis E

Answer

Correct answer : Hepatitis C

Explanation:

Hepatitis C is associated with an approximate two-fold increased risk of post-transplant diabetes mellitus. Treating the condition with clearance of the virus can substantially reduce this risk.

Reference:

- Fabrizi F, Messa P, Martin P, Takkouche B. Hepatitis C virus infection and post-transplant diabetes mellitus among renal transplant patients: a meta-analysis. Int J Artif Organs. 2008 Aug;31(8):675-82. doi: 10.1177/039139880803100801. PMID: 18825640.

Question 192

The DAPA-HF study (NEJM 2019) randomised ~4700 patients with heart failure and reduced ejection fraction to either dapagliflozin (10mg daily) or placebo in addition to conventional heart failure treatments. The primary end-point of the trial was a composite of worsening heart failure or cardiovascular death.

Which of the following was demonstrated in this study?

- **A)** A significant reduction of the primary end-point was demonstrated only in sub-group analysis within the group with type 2 diabetes
- **B)** There was a significant reduction in cardiovascular death but no difference in worsening of heart failure in those subjects treated with dapagliflozin versus placebo
- **C)** There was a significant reduction in the primary end-point but a significant increase in serious adverse events associated with dapagliflozin versus placebo
- **D)** There was a significant reduction in the primary end-point in those patients treated with dapagliflozin versus placebo
- **E)** There was a small but non-significant reduction in the primary end-point in those treated with dapagliflozin versus placebo

Answer

Correct answer : There was a significant reduction in the primary end-point in those patients treated with dapagliflozin versus placebo

Explanation:

SGLT-2 inhibitors have been extensively adopted in the treatment of patients with type 2 diabetes following studies such as EMPA-REG which revealed significant improvements in glycaemic control but also reductions in cardiovascular risk in addition to conventional treatments. The role of SGLT-2 inhibitors has been further extended to patients with heart failure associated with a reduced ejection fraction following landmark studies such as the one above – DAPA-HF published in the NEJM in late 2019. The study revealed the following as described in the abstract:

‘Over a median of 18.2 months, the primary outcome occurred in 386 of 2373 patients (16.3%) in the dapagliflozin group and in 502 of 2371 patients (21.2%) in the placebo group (hazard ratio, 0.74; 95% confidence interval [CI], 0.65 to 0.85; P<0.001). A first worsening heart failure event occurred in 237 patients (10.0%) in the dapagliflozin group and in 326 patients (13.7%) in the placebo group (hazard ratio, 0.70; 95% CI, 0.59 to 0.83). Death from cardiovascular causes occurred in 227 patients (9.6%) in the dapagliflozin group and in 273 patients (11.5%) in the placebo group (hazard ratio, 0.82; 95% CI, 0.69 to 0.98); 276 patients (11.6%) and 329 patients (13.9%), respectively, died from any cause (hazard ratio, 0.83; 95% CI, 0.71 to 0.97). Findings in patients with diabetes were similar to those in patients without diabetes. The frequency of adverse events related to volume depletion, renal dysfunction, and hypoglycaemia did not differ between treatment groups.’

In consequence, SGLT-2 inhibitors are increasingly being adopted for the treatment of such patients. Such conclusions regarding class effect have been supported with the use of empagliflozin in the EMPEROR-REDUCED study showing similar reductions in mortality and morbidity in subjects with heart failure.

References:

- McMurray, J.J., Solomon, S.D., Inzucchi, S.E., Køber, L., Kosiborod, M.N., Martinez, F.A., Ponikowski, P., Sabatine, M.S., Anand, I.S., Belohlávek, J. and Böhm, M., 2019. Dapagliflozin in patients with heart failure and reduced ejection fraction. New England Journal of Medicine, 381(21), pp.1995-2008.
- Packer, M., Anker, S.D., Butler, J., Filippatos, G., Pocock, S.J., Carson, P., Januzzi, J., Verma, S., Tsutsui, H., Brueckmann, M. and Jamal, W., 2020. Cardiovascular and renal outcomes with empagliflozin in heart failure. New England Journal of Medicine, 383(15), pp.1413-1424.

Question 1

A 20-year-old lady presented to Accident and Emergency department with abdominal pain, nausea and vomiting. She has a 5 year history of type 1 diabetes with poor adherence to her therapy. Her current insulin regimen comprises insulin glargine and novorapid via a basal bolus regimen. On examination she is dehydrated and breathing deeply, her blood pressure is 98/66 mm/hg and her pulse is 105 bpm.
Investigations-

		Normal Ranges
Plasma glucose	21.2 mmol/l	(<7.8)
pH	6.9	(7.35 - 7.45)
pCO2	3.2 kPa	(4.7 - 6)
pO2	12.1 kPa	(9.5 - 13)
Serum bicarbonate	5.2 mmol/l	(22 - 27)
Haemoglobin	15.9 g / dl	(12 - 16)
wCC	21.1 X 109	(4 - 11)

Which of the following is a feature of the pathophysiology of diabetic ketoacidosis?

- **A)** Acetoacetate is metabolized to beta-hydroxybutyrate
- **B)** Acidaemia is the primary cause of intracellular potassium loss
- **C)** Hepatic glucose production reaches a plateau within 4 hours of insulin withdrawal
- **D)** Hepatic glucose production rises gradually over the first 6 - 8 hours following insulin withdrawal
- **E)** Insulin deficiency combined with cortisol and catecholamine excess is the main cause of ketone body formation

Answer

Correct answer : Hepatic glucose production reaches a plateau within 4 hours of insulin withdrawal

Diabetic ketoacidosis is an extension of the normal fasting state. Hepatic glucose production rises rapidly over the first 2 – 4 hours following insulin withdrawal reaching a plateau after around 4 hours. These changes correlate with the initial acute rise in glucagon concentrations, with other counter-regulatory hormones being little affected initially. Basal hepatic glucose production in DKA is approximately twice that in stable diabetic patients, with a much smaller decrease in peripheral glucose utilisation. Lack of insuliswitch fatty acid metabolism. Beta-hydroxybutyrate is produced in excess and is subsequently metabolised to acetoacetate which is detected in urine ketone analysis by dip stick testing. Glucagon levels also further enhance fatty acid oxidation. Cortisol and catecholamines directly stimulate lipolysis. Glucagon is of particular importance as ketone body levels rise early, with a continuous increase over 10 – 12 hours. Acidaemia, combined with hyperglycaemia and hyperglucagonaemia promote intracellular loss of potassium. The final serum potassium concentration largely depends on the rate of urinary potassium loss. Platelet secretory activity is often increased in DKA, but aggregation decreased. Neutrophil count is also commonly raised and correlates with ketone body levels, so does not necessarily imply underlying infection.

Question 2

A 70-year-old male is admitted complaining of involuntary movements on the left side of the body. These symptoms have deteriorated over the last 3 weeks. He has a 10-year history of type 2 diabetes for which he takes ramipril 10mg/d, metformin 1g bd, sitagliptin 100mg /d and atorvastatin 20mg daily.

On examination, his pulse is 80 bpm reg, blood pressure 136/88 mmHg. He has writhing movements on the left limbs with some occasional left arm and leg flinging movements. Neurological examination is otherwise normal, with flexor plantars and normal reflexes.

Investigations:

Test	Result	Normal Range
FBC	Normal	
U+Es	Normal	
Glucose	25.9 mmol/l	(3.5-5.5)
HbA1c	88 mmol/mol	(<48) (10.2%)
CT Head Report	Evidence of small vessel disease. Nil acute	
Blood ketones	0.5 mmol/l	(<0.6)

Which of the following is the likely diagnosis?

- **A)** Diabetic hemi-chorea hemi-ballism syndrome
- **B)** Drug-induced chorea
- **C)** Haemochromatosis
- **D)** Stroke
- **E)** Wilson’s disease

Answer

Correct answer : Diabetic hemi-chorea hemi-ballism syndrome

Explanation:

This is a typical history of the rare but well-described non-ketotic hyperglycaemic (diabetic) hemi-chorea hemi-ballism syndrome characterised by continuous, irregular, and involuntary jerky movements of one side of the body, often the result of a focal lesion of the contralateral basal ganglia. The condition is associated with poor glycaemic control, as in this case and, improved glycaemic control is associated with improvement and resolution of symptoms. The pathophysiology of the disorder is associated with relative ischaemia, possibly a result of hyperviscosity within the striatum. A CT scan may be normal or reveal densities in the putamen/arcuate nucleus, so an MRI is often required and demonstrates T1 hyperintensity in the contralateral putamen.

Reference:

- Al Montasir, A. and Sadik, M.H., 2013. Hemichorea-hemiballism in a nonketotic diabetic patient. Journal of family medicine and primary care, 2(3), p.296.

Question 3

A 21-year-old lady with a 10-year history of type 1 diabetes has a most recent Hba1c of 7.8% <6% and is admitted to accident and emergency following an overdose of her basal insulin. On examination, she is conscious but pale and sweaty, her blood pressure is 96 66 mmhg, her pulse is 135 beats per minute and her plasma glucose is 1.8.

At what plasma glucose level would you expect significant autonomic counter-regulatory responses to develop in patients with type 1 diabetes?

- **A)** ≤1 mmol/l
- **B)** ≤1.5 mmol/l
- **C)** ≤2 mmol/l
- **D)** ≤2.5 mmol/l
- **E)** ≤3.5 mmol/l

Answer

Correct answer : ≤3.5 mmol/l

Autonomic counter-regulatory responses, including beta adrenergic stimulation and catecholamine secretion, commence at a threshold plasma glucose level ≤ 2.5 mmol/l in non-diabetic individuals and often occur at a higher level in patients with diabetes. Counter-regulatory responses such as increased glucagon secretion and mobilisation of glucose stores in muscle and liver usually commence at threshold plasma glucose levels of 3.5 – 3.8 mmol/l. Hypoglycaemia and counter-regulation

Question 4

An 18-year-old young lady is admitted to the acute medical unit with nausea, vomiting and abdominal pain. She gives a history of approximately 5 kg weight loss over the past month to two months and also complains of persistent thirst and polyuria over the last 2 weeks. On examination her blood pressure is 105/65 mmHg, her pulse is 92 beats per minute and her body weight is 64.8 kg.
Investigations reveal:

		Normal Ranges
Plasma glucose	21.7 mmol/l	(3.5 - 5.5)
pH	7.03	(7.35 - 7.45)
pCO2	2.9 Kpa	(4.6 - 6)
pO2	15.6 Kpa	(11.1 - 14.4)
Bicarbonate	4.6 mmol/l	(22 - 27)
Haemoglobin	14.9 g/ dl	
WCC	17.9 X 109	(4 - 11)

Which of the following is a feature of the clinical management of diabetic ketoacidosis?

- **A)** Administer bicarbonate if the PH is below 7.1
- **B)** Aim to give 8 litres of hypotonic fluid during the first 10 hours
- **C)** IV antibiotics should be administered if neutrophilia is present
- **D)** Total body potassium is reduced by up to 500 mmol
- **E)** When blood glucose falls below 8 mmol/L, 5% dextrose should be substituted in place of normal saline

Answer

Correct answer : Total body potassium is reduced by up to 500 mmol

Fluid replacement is the cornerstone of therapy in the management of DKA. The total body deficit of fluid is around 5 - 8 litres and rehydration by reopening renal perfusion may on its own reduce blood glucose by up to 2%. JBDS guidelines recommend crystalloids and the fluid of choice is normal saline. The rate of fluid replacement depends on individual factors such as heart failure and liver failure etc. Once the glucose has fallen to around 14 mmol/l, infusion of 10% glucose should be substituted for saline. This will allow continued infusion of insulin to correct metabolic acidosis and ketosis; saline may be given simultaneously if the patient is still dehydrated. Adequarte fluid and insulin therapy would resolve acidosis. Administration of bicarbonate is not recommended as per the JBDS guidelines. Antibiotics should only be administered if an infective aetiology or focus can be identified. As a result of both acidosis and insulin deficiency there is a total body potassium deficit of up to 1000 mmol. Hence with rehydration, insulin replacement and correction of acidosis resulting in further potassium loss with restoration of urine flow, hypokalemia is a major cause of death in ketoacidosis.

Question 5

An 80-year-old male is admitted after being found collapsed at home by his daughter.
He has a previous history of diet controlled type 2 diabetes and cerebrovascular disease. On examination, he is drowsy and dehydrated, his blood pressure is 106/56 mm/Hg and he has a a pulse rate of 123 beats per minute.
Investigations reveal:

		Normal Ranges
Plasma glucose	56.5 mmol/l	(<7.8)
Sodium	165 mmol/l	(135 - 146)
Potassium	6.3 mmol/l	(3.4 - 5.1)
Urea	18.1 mmol/l	(3 - 7)
Creatinine	165 umol/l	(68 - 118)
Haemoglobin	13.9 g/ dl	(12 - 16)
WCC	19.6 X 10^9	(4 - 11)
pH	7.24	(7.35 - 7.45)
pCO2	4.3 Kpa	(4.6 - 6)
p02	12.1 Kpa	(11.1 - 14.4)
Bicarbonate	14.9 mmol/l	(22 - 27)

Which of the following best reflects the mortality associated with the above condition?

- **A)** 0-10%
- **B)** 10-20%
- **C)** 20-30%
- **D)** 30-40%
- **E)** ~50%

Answer

Correct answer : ~50%

The mortality in patients with Hyperosmolar Hyperglycemic state(HHS) is very high, approaching up to 50% in some series, with infection being the commonest precipitating factor, accounting for up to 80% of cases. Fluid depletion in HHS is up to 10 litres with the aim of fluid replacement therapy being to replace this deficit over 24 – 48 hours. The pathophysiology of HHS involves a relative insulin deficiency combined with grossly elevated glucagon concentrations, resulting in a marked increase in hepatic glucose output. Due to the relative insulin deficiency peripheral glucose utilisation is reduced and lipolysis relatively unrestrained leading to increased NEFA concentrations and lipid oxidation rates which further stimulates hepatic gluconeogenesis. Unlike DKA, significant ketosis is absent in HONK, despite similar levels of circulating insulin. Various mechanisms have been suggested, with the most convincing suggestion being that hyperosmolality and dehydration per se inhibit ketogenesis. Correction of hyperglycaemia with infused insulin should be gradual, with the aim of reducing blood glucose by 4 to 6 mmol/l/hour. More rapid correction of hyperglycaemia may result in cerebral oedema.

Chung ST, Perue GG, Johnson A, Younger N, Hoo CS, Pascoe RW, Boyne MS. Predictors of hyperglycaemic crises and their associated mortality in Jamaica. Diabetes Res Clin Pract. 2006 Aug;73(2):184-90. https://abcd.care/sites/abcd.care/files/resources/JBDS_IP_HHS_Adults.pdf

Question 6

A 26-year-old lady is reviewed in the clinic. She has a 10 year history of type 1 diabetes and admits to frequently missing insulin doses. Her current medication includes insulin glargine 42 units at night and novorapid 12 units prior to each meal. On examination her BMI is 21 kg/m2 and her blood pressure is 105 / 65 mmHg.
Investigations reveal:

		Normal Ranges
HbA1c	94.5 mmol/l(10.8%)	(<48mol/mol (6.5%))
Total cholesterol	4.1 mmol/l	(<5)
Plasma triglyceride	1.9 mmol/l	(0.9 - 2.2)
TSH	0.65 mu / l	(0.32 - 5.5)
Urine ketones	+++	
Urine glucose	+++	

Which of the following is a feature of urine ketone testing?

- **A)** Heavy ketonuria implies the need for insulin initiation when identified in patients with type 2 diabetes
- **B)** Ketonuria correlates closely with degree of acidosis in diabetic ketoacidosis
- **C)** Ketonuria resolves with correction of acidosis in diabetic ketoacidosis
- **D)** Urine ketone stix measure acetoacetate in the urine
- **E)** Urine ketone stix measure beta-hydroxybutyrate levels in the urine

Answer

Correct answer : Urine ketone stix measure acetoacetate in the urine

Urine ketone testing measures acetoacetate in urine which is produced by metabolism of beta-hydroxybutyrate. Ketonuria persists despite correction of acidaemia in patients with ketoacidosis and does not correlate with the degree of acidosis. Ketonuria is not a marker of absolute insulin deficiency and may occur as a normal response to exercise or fasting.

Question 7

A 33-year-old woman is currently 34 weeks pregnant. She was commenced on continuous subcutaneous insulin infusion at the end of the first trimester after developing severe recurrent hypoglycaemic episodes. Her HbA1c has been 5.8% and she has had an occasional hypoglycaemic episode but generally these have been mild and she has been able to manage these herself. She telephones your department as during the last 24 hours she has developed recurrent severe hypoglycaemic episodes such that she is continually taking lucozade to prevent this despite dramatically reducing her insulin rates. How would you advise her?

- **A)** Advise her to come into hospital immediately for assessment for urgent delivery of her baby.
- **B)** Advise that the pump be re-sited at least 10cm from the current insertion site
- **C)** Remove her pump and repeat the process of drawing up the insulin and priming the pump and using a new giving set and cannula in case of an error
- **D)** Remove the pump and revert to insulin via a pen until a new pump is able to be delivered urgently
- **E)** Reduce all basal rates to 50% and halve the insulin to carbohydrate ratio

Answer

Correct answer : Advise her to come into hospital immediately for assessment for urgent delivery of her baby.

Placental insufficiency can present in diabetes as severe recurrent unwarranted hypoglycaemia. This should always be regarded as an emergency in the third trimester as this may herald placental insufficiency and prompt action and delivery may prevent intrauterine death. Only after placental insufficiency has been excluded should other causes of hypoglycaemia be explored.

Question 8

A 62-year-old woman with acute symptomatic hyponatraemia likely due to SIADH and associated with drowsiness is considered to be appropriate for immediate treatment with hypertonic saline. Her serum sodium is 115 mmol/l. What is the target sodium to which you would treat this patient over the next 1hr?

- **A)** 116 mmol/l
- **B)** 120 mmol/l
- **C)** 125 mmol/l
- **D)** 130 mmol/l
- **E)** 135 mmol/l

Answer

Correct answer : 120 mmol/l

A decision has been taken to treat this patient with hypertonic saline as she has acute symptomatic hyponatraemia which reflects underlying cerebral oedema. In this context, treatment with 150 ml 3% hypertonic saline given over 20minutes is recommended as per the guidelines. The target sodium by which one should elevate the sodium is 5 mmol/l over the first hour. The increase in sodium should be then limited to 10 mmol/l over the next 24hrs based on a clinical improvement.

Guidelines

European Journal of Endocrinology (2014) Clinical practice guideline on diagnosis and treatment of hyponatraemia

Question 9

You are called to see a 42-year-old male patient on the neurosurgical ward. He was admitted with a head injury 3 days ago which required only observation. However, he has become more confused in the last 12 hours and his most recent U+Es performed this morning reveal:

		Normal Ranges
Sodium	125 mmol/l	(134-144)
Potassium	4.5 mmol/l	(3.5-5.5)
Urea	6.8 mmol/l	(3-8)
Urine Osmolality	620 mosmol/l	
Urine Sodium	125 mmol/l	

Checking through his records, the previous days his U+Es were normal. He had been allowed to eat and drink normally and had stopped IV fluids 2 days ago. He was on dexamethasone the dose of which had been reduced to 4mg daily from 8 mg daily over the last day but he was on no other treatment.

On examination, he had Glasgow Coma Scale of 14, though seemed confused with him being disorientated. Oxygen saturations were 97% on air and his blood pressure was 110/80 with a pulse of 88 bpm.

Which of the following is the most likely diagnosis?

- **A)** Acute hypoadrenalism
- **B)** Cerebral salt wasting
- **C)** Pituitary apoplexy
- **D)** Syndrome of inappropriate ADH secretion
- **E)** Type IV renal tubular acidosis

Answer

Correct answer : Cerebral salt wasting

The most likely diagnosis in this patient with head injury who then develops acute symptomatic hyponatraemia and grossly elevated urine sodium is cerebral salt wasting. The grossly elevated urine sodium (>100) is highly suggestive as the sodium is usually less with SIADH. Similarly with SIADH, there is a dilutional element so urea and potassium typically reflect this dilution being themselves low normal, in contrast to CSW where there is hypovolaemia and hence higher concentrations. Hypoadrenalism is an incorrect answer as the patient is already on a high dose of steroids – dexamethasone 4 mg/d.

References

- Cerebral Salt Wasting Medscape

Question 10

A 53-year-old man is admitted with a 3 day history of left leg pain and fever. He has an 8 year history of type 2 diabetes for which he takes metformin and gliclazide together with ramipril and simvastatin.

On examination his BMI is 32.3 kg/m^2, his temperature is 38.5C, pulse 90 bpm and his blood pressure 120/80 mmHg. His left leg is swollen to mid-calf, the skin is red and inflamed with a clear demarcation just below the knee. He has some onycholysis of the left toe nails with some maceration between the toes. His peripheral pulses are all palpable.

Results show:

		Normal Ranges
Sodium	136 mmol/l	(134-144)
Potassium	4.2 mmol/l	(3.5-5.5)
Urea	12.1 mmol/l	(3-8)
Creatinine	128 micromol/l	(50-100)
Haemoglobin	13.3 g/l	(120-160)
White cell count	$12.8x10^9$/l	(3-10)
Platelets	$158x10^9$/l	(140-450)
C-reactive protein	135 mg/dl	(<5)
Glucose	12.3 mmol/l	
HbA1c	61.7 mmol/l(7.8%)	(<48mol/mol (6.5%))

Which of the following would be the most appropriate treatment for this patient?

- **A)** IV flucloxacillin
- **B)** Oral amoxicillin
- **C)** Oral ciprofloxacin
- **D)** Oral flucloxacillin

- **E)** IV Vancomycin

Answer

Correct answer : IV flucloxacillin

This patient has a clinical class II to class III cellulitis with systemic upset associated with a comorbidity. The vast majority of cases of cellulitis are due to beta haemolytic strep or S. aureus. Therefore, flucloxacillin is the treatment of choice in this setting and recommended in guidelines as IV treatment in Class II-III patients. In subjects allergic to beta lactams, clarithromycin/clindamycin can be used.

- Guidance on management of cellulitis in adults

Question 11

A 62-year-old woman is referred to the medical intake with tingling and paraesthesia. The patient has been aware of deteriorating symptoms for one week. The GP asks whether this is a stroke. She has a background history of type 2 diabetes, hypertension and GORD for which she takes omeprazole, metformin, sitagliptin, simvastatin, ramipril and amlodipine. On examination there is little of note.
Investigations reveal:

Calcium	2.06 mmol/l (2.2-2.6)
Magnesium	0.3 mmol/l (0.7-1)
LFTs	Normal

You see on the computer that a 25OHD level checked 1 month before by the GP reveals a level of 18 nmol/l (>50).
Which of the following is the likely cause of this patient's presentation?

- **A)** Diabetic autonomic neuropathy
- **B)** Metformin
- **C)** Omeprazole
- **D)** Sitagliptin
- **E)** Vitamin B deficiency

Answer

Correct answer : Omeprazole

This patient has a hypocalcaemia associated with a severe hypomagnesaemia. This is likely due to the omeprazole, which results in increased GI magnesium losses. The hypomagnesaemia impairs the calcium sensing on the parathyroid cells; hence, this results in an induced hypoparathyroidism with hypocalcaemia. It is a good diagnosis to make but is often not appreciated.

< />

- PPI induced hypoparathyroidism

Question 12

A 30-year-old female is admitted with a 2 day history of abdominal pains and general deterioration. She has a background history of type 1 diabetes for which she takes basal bolus insulin regime consisting of a long acting insulin (20 iu) in the evening and thrice daily short acting insulin (10-12 iu) with each meal. She has continued to take her insulin but has become iller, being nauseous with vomiting associated with a some abdominal pain.
On examination, she appears dehydrated, has a pulse of 98 bpm reg and a blood pressure of 108/76 mmHg. Her Glasgow coma scale is 15 and she has oxygen saturations of 98% on air. Abdominal examination reveals nothing overt with just diffuse tenderness.
Her results reveal the following:

		Normal Ranges
Glucose	23.7 mmol/l	(3.5-5.5)
Sodium	144 mmol/l	(134-144)
Potassium	3.0 mmol/l	(3.5-5.5)
Urea	8.3 mmol/l	(3-8)
Creatinine	Creatinine	
pH	7.28	
pO2	14.4kPa	
PCO2	3.5 kPa	
Bicarbonate	15 mmol/l	

Which of the following is the most appropriate initial management for this patient's hyperglycaemia?

- **A)** Fixed rate IV insulin infusion of 0.1iu/kg/hr
- **B)** Give 15 units of SC short acting insulin together with 10 units of long acting insulin
- **C)** Initial priming bolus dose of IV insulin followed by sliding scale insulin
- **D)** Sliding scale IV insulin infusion
- **E)** Sliding scale insulin with pre-meal insulin of 3-5 units plus continue with 24 units of basal insulin

Answer

Correct answer : Fixed rate IV insulin infusion of 0.1iu/kg/hr

This patient has developed diabetic ketoacidosis as evidenced by the low bicarbonate,(15mmol/l) and pH(less than 7.30). Guidelines recommend the use of an iv fixed rate insulin infusion regime consisting of 0.1 iu/kg/hr and to continue the patient's usual long acting insulin agent.

reference:

- Joint British Societies Diabetes Care Group DKA Guidelines

Question 13

A 30-year-old female is admitted with a 2 day history of abdominal pains and general deterioration. She has a background history of type 1 diabetes for which she takes basal bolus insulin regime consisting of a long acting insulin (20 iu) in the evening and thrice daily short acting insulin (10-12 iu) with each meal. She has continued to take her insulin but has become iller, being nauseous with vomiting associated with a diffuse abdominal pain.
On examination, she appears dehydrated, has a pulse of 98 bpm reg and a blood pressure of 108/76 mmHg. Her Glasgow coma scale is 15 and she has oxygen saturations of 98% on air. Abdominal examination reveals nothing overt with just diffuse tenderness.
Her results reveal the following:

		Normal Ranges
Glucose	23.7 mmol/l	(3.5-5.5)
Sodium	144 mmol/l	(134-144)
Potassium	3.0 mmol/l	(3.5-5.5)
Urea	8.3 mmol/l	(3-8)
Creatinine	105 micromol/l	50-100)
pH	7.28	
pO2	14.4 kPa	
PCO2	3.5 kPa	
Bicarbonate	15 mmol/l	

Which of the following is the most appropriate initial management for this patient?

- **A)** 100mls 8.4% sodium bicarbonate over 30 mins, together with 1l Normal saline with 20 mmol potassium chloride over 1hr
- **B)** 1l 5% dextrose given over 1 hr
- **C)** 1l Hartmann’s solution given over 2 hrs
- **D)** 1l Normal saline given over 2 hr
- **E)** 1l Normal saline with 20 mmol potassium chloride given over 1 hr

Answer

Correct answer : 1l Normal saline with 20 mmol potassium chloride given over 1 hr

In this patient who has diabetic ketoacidosis, the most appropriate treatment for immediate IV resuscitation is 1l of Normal saline given over the first hour and, in view of the low potassium, potassium chloride should also be given as this will fall quite abruptly when the insulin regimen is started.

Reference:

- Joint British Societies Diabetes Care Group DKA Guidelines

Question 14

A 41-year-old woman is admitted with a 24-hour history of nausea and vomiting. She has a history of Addison's disease and type 1 diabetes for which she takes hydrocortisone 10 mg bd and twice-daily mixed insulin 24 iu in the morning and 18 iu in the late afternoon.
On examination she appears dehydrated and unwell. Her temperature is 37C, blood pressure 90/66 mmHg and pulse 100 bpm reg. Her Glasgow Coma Scale is 15 and there are no significant findings on general examination.
Investigations reveal the following:

		Normal Ranges
Glucose	9.9 mmol/l	(3.5-5.5)
Sodium	129 mmol/l	(134-144)
Potassium	5.5 mmol/l	(3.5-5.5)
Urea	8.2 mmol/l	(3-8)
Ketones on meter	0.7 mmol/l	(<1.5)

Which of the following would be the most appropriate treatment for this patient?

- **A)** 100mcg oral fludrocortisone
- **B)** 1l N saline over 1hr
- **C)** 100 mg IV hydrocortisone as a bolus
- **D)** Fixed rate insulin infusion 0.1 iu/kg/hr
- **E)** IV insulin sliding scale

Answer

Correct answer : 100 mg IV hydrocortisone as a bolus

This patient appears to have a hypoadrenal crisis probably precipitated by the inability to retain the oral hydrocortisone. In this case the glucose less than 10 and the absence of ketones on the ketone meter makes a diagnosis of DKA unlikely. The most appropriate approach is to treat this patient with 100 mg IV hydrocortisone.

Reference:

- Guidelines from the endocrine society

Question 15

A 55-year-old man is admitted through MAU with 1 week history of deteriorating weakness and more recent nausea. His background includes a 10-year history of diabetes and hypertension. He is taking gliclazide 80mg bd, bendrofluazide 2.5mg/d, atorvastatin 10mg/d and ramipril 10 mg/d.

On examination he appears ill and weak. His temperature is 37 C and oxygen saturation is 97% on air. His blood pressure is 154/100 mmHg, heart rate 92 bpm reg and respiratory rate is 22/min.

Results:

		Normal Ranges
Sodium	141 mmol/l	(134-144)M=
Potassium	7.6 mmol/l	(3.5-5.5)
Urea	19 mmol/l	(3-8)
Creatinine	350 micromol/l	(50-100)
pH	7.36	
Bicarbonate	20 mmol/l	

His ECG reveals some QRS widening and tenting of T waves.

Which of the following is the most appropriate initial treatment for this man?

- **A)** 10 mg nebulised salbutamol
- **B)** 10 ml 10% IV calcium gluconate as a stat dose
- **C)** 100 ml of 8.4% sodium bicarbonate given over 30 mins
- **D)** 50 ml IV 50% dextrose plus 10 iu insulin given over 10 mins
- **E)** Oral calcium resonium

Answer

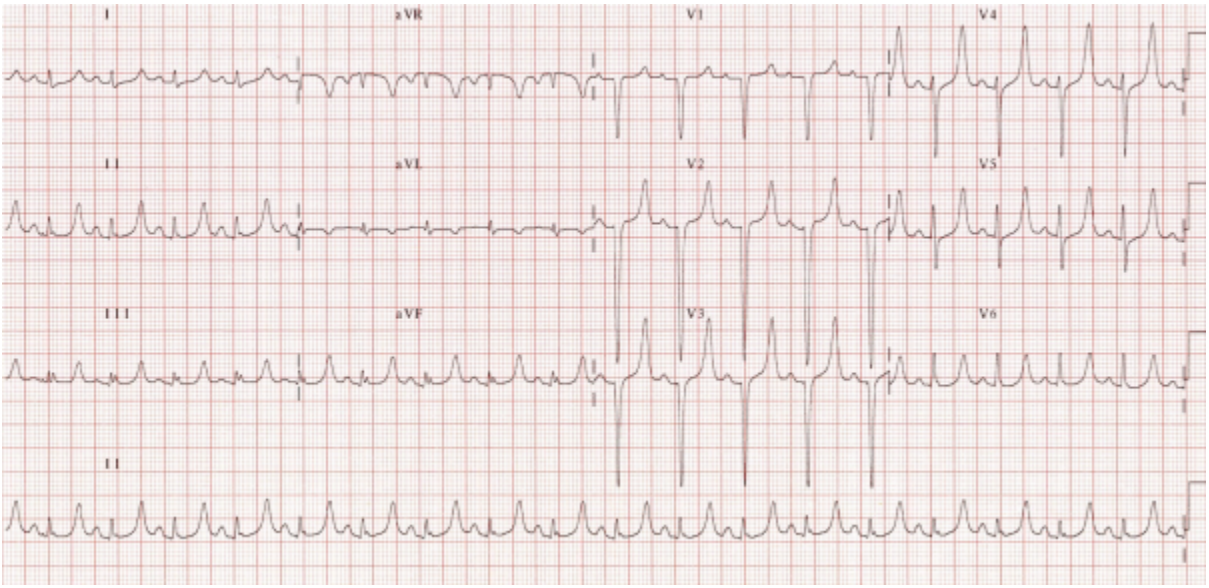
Correct answer : 10 ml 10% IV calcium gluconate as a stat dose

This patient has severe and life threatening hyperkalaemia as determined by the potassium above 6.5 and the widened QRS complexes and tented T waves on the ECG. The most important initial step is protection of the heart – hence the patient should receive 10 mls of 10 %calcium gluconate and the ECG should be repeated to look for improvement. At the same time, the insulin and dextrose infusion should be started, although this may take 1 hour to take effect by reducing the potassium. In this case, the ACE inhibitor needs to be stopped and in conjunction with the acute kidney injury may be the precipitant.

ReferenceRenal Society Guidelines on treating hyperkalaemia

Question 16

This is the ECG obtained on a 77-year-old man with type 2 diabetes who was admitted with lethargy and tiredness.



What does the ECG suggest?

- **A)** Hypercalcaemia
- **B)** Hyperkalaemia
- **C)** Hypocalcaemia
- **D)** Hypokalaemia
- **E)** Hypothermia

Answer

Correct answer : Hyperkalaemia

This ECG shows tented T waves and p waves with a tachycardia suggestive of hyperkalaemia.

Question 17

A 48-year-old man is admitted acutely with a one-week history of feeling increasingly unwell and tired. He was diagnsed with type 2 Diabetes aproximately 8 months ago for which he takes metformin 1g bd and gliclazide 80mg bd. His last HbA1c was 10.1%.
On examination he appears dehydrated and unwell. His temperature is 37C , blood pressure 116/70 mmHg and a pulse of 102 bpm. Oxygen saturation is 98% on air and he has a respiratory rate of 22/min.blood ketones 5mmol
Blood results reveal:

		Normal Ranges
Sodium	147 mmol/l	(134-144)
Potassium	5.5 mmol/l	(3.5-5.5)
Urea	15.5 mmol/l	(3-8)
Glucose	24.5 mmol/l	(3.5-5.5)
pH	7.28	(7.35-7.45)
Bicarbonate	10 mmol/l	(22-28)

Which of the following is the likely diagnosis?

- **A)** Acute kidney injury associated with ACE inhibitor
- **B)** Diabetic ketoacidosis
- **C)** Hyperosmolar hyperglycaemic state
- **D)** Type A lactic acidosis
- **E)** Type B lactic acidosis associated with metformin

Answer

Correct answer : Diabetic ketoacidosis

The most likely diagnosis is diabetic ketoacidosis (patient is acidotic) in a poorly controlled type 2 patient that may well have Latent Autoimmune Diabetes of Adulthood (LADA). Here is the history of type 2 Diabetes is short indicating that this patient likely had LADA. Lactic acidosis with metformin is very rare and the patients usually have severe renal impairment. There is likely to be ketones present on POCT testing. This is not HHS as plasma osmolality is usually above 320 and glucose above 33 with a pH >7.3.

Question 18

An 81-year-old man is admitted acutely with a one-week history of feeling increasingly unwell and weak. He has a history of type 2 diabetes for which he takes metformin 1g bd and gliclazide 80mg bd. His last HbA1c was 10.1%. He also takes ramipril and simvastatin.
On examination he appears dehydrated and unwell. His temperature is 37C , blood pressure 116/70 mmHg and a pulse of 102 bpm. Oxygen saturation is 98% on air and he has a respiratory rate of 22/min.
Blood results reveal:

		Normal Ranges
Sodium	155 mmol/l	(134-144)
Potassium	4.2 mmol/l	(3.5-5.5)
Urea	20.5 mmol/l	(3-8)
Glucose	37.2 mmol/l	(3.5-5.5)
pH	7.35	(7.35-7.45)
Bicarbonate	18 mmol/l	(22-28)
Ketones	1.8 mmol/l	(<1.5)

Which of the following is the likely diagnosis?

- **A)** Acute kidney injury associated with ACE inhibitor
- **B)** Diabetic ketoacidosis
- **C)** Hyperosmolar hyperglycaemic state
- **D)** Severe dehydration with acute kidney injury
- **E)** Type B lactic acidosis associated with metformin

Answer

Correct answer : Hyperosmolar hyperglycaemic state

The most likely diagnosis is HHS as plasma osmolality 376 mosmol/l with glucose above 33, bicarbonate above 15 and a pH >7.3. A trace of ketones may be noted (<3).

Reference:

- Hyperosmolar hyperglycaemic state

Question 19

A 62-year-old woman attends A&E feeling unwell. She is lethargic, has had occasional episodes of abdominal pain and is clinically dehydrated. She has a recent history of metastatic breast cancer with bony involvement, for which she is receiving palliative treatment. Her results reveal:

		Normal Ranges
Sodium	144 mmol/l	(134-144)
Potassium	3.3 mmol/l	(3.5-5.5)
Urea	10.8 mmol/l	(3-8)
Creatinine	255 micromol/l	(50-100)
Calcium	4.1 mmol/l	(2.2-2.6)

Which of the following is the most appropriate initial treatment for this patient?

- **A)** IM calcitonin
- **B)** IM denosumab
- **C)** IV hydrocortisone
- **D)** IV N saline – 1l over 2hrs initially
- **E)** IV pamidronate

Answer

Correct answer : IV N saline – 1l over 2hrs initially

The most appropriate initial treatment for this patient is IV rehydration with N saline (4-6l over 24hrs). Once rehydration is considered adequate, the patient can then be treated with IV bisphosphonates such as pamidronate, but caution needs to be exercised with the acute kidney injury. In this case the likely cause is metastatic bone disease, so regular bisphosphonate infusions may be required.

Management of Hypercalcaemia

Question 20

A 70-year-old male is admitted complaining of involuntary movements on the left side of the body. These symptoms have deteriorated over the last 3 weeks. He has a 10-year history of type 2 diabetes for which he takes ramipril 10mg/d, metformin 1g bd, sitagliptin 100mg /d and atorvastatin 20mg daily.

On examination, his pulse is 80 bpm reg, blood pressure 136/88 mmHg and BMI 28 kg/m^2. He has writhing movements on the left limbs with some occasional left arm and leg flinging movements.

Neurological examination is otherwise normal with flexor plantars and normal reflexes.

Investigations:

Test	Result	Normal Range
FBC	Normal	
U+Es	Normal	
Glucose	25.9 mmol/l	(3.5-5.5)
HbA1c	88 mmol/mol	(<48) (10.2%)
Blood ketones	0.5 mmol/l	(<0.6)
CT Head Report	Small vessel disease. Mildly increased density in right basal ganglia	

Which of the following is the most appropriate approach to the management of this patient?

- **A)** Commence tetrabenazine
- **B)** Commence topiramate
- **C)** Commence variable rate insulin infusion
- **D)** Commence variable rate insulin infusion with IV diazepam
- **E)** Stop sitagliptin; commence gliclazide

Answer

Correct answer : Commence variable rate insulin infusion

Explanation:

This is a typical history of the rare but well-described non-ketotic hyperglycaemic (diabetic) hemi-chorea hemi-ballism syndrome characterised by continuous, irregular, and involuntary jerky movements of one side of the body, often the result of a focal lesion of the contralateral basal ganglia. It usually affects elderly women, and there is an Asian preponderance. The condition is associated with poor glycaemic control, as in this case and, improved glycaemic control is associated with improvement and resolution of symptoms. There is no ketosis. The pathophysiology of the disorder is associated with relative ischaemia, possibly a result of hyperviscosity within the striatum. CT may be normal or reveal densities in the putamen/ arcuate nucleus so MRI is often required and demonstrates T1 hyperintensity in the contralateral putamen.

Explanation:

- Al Montasir, A. and Sadik, M.H., 2013. Hemichorea-hemiballism in a nonketotic diabetic patient. Journal of family medicine and primary care, 2(3), p.296.

Question 21

A 71-year-old woman was admitted with a two day history of increasing fatigue and decreasing level of consciousness. She had otherwise been well. She had type 2 diabetes for which she was being treated with metformin 500 mg bd, empagliflozin 10 mg daily, ramipril 10mg daily and atorvastatin 10 mg daily. On examination she had a temperature of 38C, a blood pressure of 100/70 mmHg and a pulse of 100 bpm with a respiratory rate of 28/min. Her Glasgow Coma Scale score was 12. There was nil of note on abdominal, respiratory, neurological or cardiovascular examination. Results revealed:

Test	Result	Normal range
Haemoglobin	12 g/dl	12-16
White cell count	14.5x109/l	3.5-10
Platelet	210x109/l	150-400
Sodium	140 mmol/l	134-144
Potassium	5 mmol/l	3.5-5
Creatinine	210 micromol/l	50-100
Urea	8.3 mmol/l	3-8
Glucose	14.5 mmol/l	3.5-5.5
pH	7	7.35-7.45
Bicarbonate	7 mmol/l	22-28
pCO2	1.9 kPa	4.5-6
pO2	14.8 kPa	10.5-13
Lactate	2.1 mmol/l	0.5-1
Ketones (on meter)	Hi	

Which of the following is the likely cause of her presentation?

- **A)** Diabetic ketoacidosis
- **B)** Drug-induced diabetic ketoacidosis
- **C)** Drug-induced lactic acidosis

- **D)** Sepsis with fasting ketosis
- **E)** Sepsis with mixed fasting ketosis/lactic acidosis

Answer

Correct answer : Drug-induced diabetic ketoacidosis

This patient has developed a severe metabolic acidosis as suggested by the low pH and low bicarbonate with some respiratory compensation. The ketones are high which is highly relevant here, particularly as the lactate is only modestly high and does not suggest lactic acidosis. A good going lactic acidosis would be above 5. Also, the glucose is only modestly elevated. This fits the picture of a drug-induced ketoacidosis due to the SGLT-2 inhibitor, empagliflozin. Whilst a very effective diabetic medication, all SGLT-2 inhibitors have been rarely implicated in euglycaemic or modestly hyperglycaemic ketoacidosis, an effect of their mechanism of action relaying on urinary glucose excretion. Often illness, fasting and vomiting exacerbate the ketosis.

Reference:Tucker, M. E., 2017. SGLT2 Inhibitors Double the Risk for Diabetic Ketoacidosis. Medscape.

Question 22

A 45-year-old man was admitted through the emergency department for an emergency appendectomy. He was known diabetic for the past 6 years, taking oral hypoglycemics with poor glycemic control. His HbA1 was 10% 1 month ago. At the time of admission, his blood glucose was 14mmol/L. He was given 7 units of subcutaneous rapidly acting analogue insulin. After 1 hour his blood glucose was re-checked and it was 13mmo/L.

Test	Result	Normal Range
Bedside urinary ketones	++	
Capillary blood ketones	2.5mmol/L	
ABGs: pH	7.37	(7.35-7.45)

What should be the most appropriate next step according to The Joint British Diabetes Societies (JBDS) guidelines?

- **A)** Cancel the emergency appendectomy, follow DKA guidelines and contact the diabetes specialist team
- **B)** Commence FRIII (fixed rate intravenous insulin infusion)
- **C)** Commence VRIII (variable-rate intravenous insulin infusion)
- **D)** Repeat the same dose of subcutaneous rapidly acting analogue insulin after 2 hours
- **E)** Repeat the subcutaneous rapidly acting analogue insulin after 2 hours, doubling the dose

Answer

Correct answer : Commence VRIII (variable-rate intravenous insulin infusion)

Explanation:

According to JBDS guidelines:

Manage hyperglycaemia in patients undergoing surgery with a short starvation period (one missed meal) as:

- If blood glucose is greater than 12mmol/L pre or post-surgery, check capillary blood ketones using an appropriate bedside monitor if available. If capillary blood ketones are greater than 3mmol/L or urinary ketones greater than +++ or greater cancel surgery, follow DKA guidelines and contact the diabetes specialist team or the on-call medical team for advice.
- For preoperative hyperglycaemia: (blood glucose greater than 12mmol/L with blood ketones less than 3mmol/L or urine ketones less than +++), for type 1 & 2 diabetics, give subcutaneous rapid-acting analogue insulin. Assume that 1 unit will drop the blood glucose by 3mmol/L. Recheck blood glucose 1 hour later to ensure it is falling. If surgery cannot be delayed or the response is inadequate, commence a VRIII.
- For postoperative hyperglycaemia: (blood glucose greater than 12mmol/L with blood ketones less than 3mmol/L or urine ketones less than +++), for type 1 and type 2 diabetics, give 0.1 units/kg of subcutaneous rapid-acting analogue insulin, and recheck blood glucose 1 hour later to ensure it is falling. Repeat the subcutaneous insulin after 2 hours if the blood glucose is still above 12mmol/L. In this situation, the insulin dose selected should take into account the response to the initial dose – consider doubling the dose if the response is inadequate. Repeat the blood glucose after another hour. If it is not falling, consider introducing VRIII.
- The aim of the VRIII is to achieve and maintain glucose levels within the target range of 6-10mmol/L, although up to 12mmol/L may be acceptable.

  This is done by infusing a constant rate of glucose-containing fluid as substrate while infusing insulin at a variable rate. The VRIII is the preferred method of controlling the surgical patient's serum glucose in the following circumstances:
- Patient with Type 1 diabetes undergoing surgery with a starvation period greater than 1 missed meal
- Patient with Type 1 diabetes undergoing surgery who has not received background insulin
- Patient with Type 2 diabetes undergoing surgery with a starvation period greater than 1 missed meal and develops hyperglyacemia (CBG >12mmol/L)
- Patients with poorly controlled diabetes as defined as an HbA1c >69mmol/mol (>8.5%)
- Most patients with diabetes requiring emergency

Reference:

- JBDS-IP (March 2016). Management of adults with diabetes undergoing surgery.

Question 23

A 55-year-old woman was admitted to the surgical department for a cholecystectomy. She has been diabetic for the past 10 years, and takes oral hypoglycemics only, with poor glycemic control. Her last HbA1c test revealed a level of 8%. Perioperatively she was commenced on insulin as VRIIII (variable-rate intravenous insulin infusion). She remained stable postoperatively, she was able to eat and drink and managed to eat one meal; however, her blood glucose remained 12-15mmol/L. In addition to restarting oral hypoglycemics, insulin was recommended before discontinuation of VRIII.

The total insulin administered via VRIII in the last 6 hours was 18 units. What should the total daily dose (TDD) in this insulin naive patient be?

- **A)** 18 units
- **B)** 24 units
- **C)** 40 units
- **D)** 60 units
- **E)** 72 units

Answer

Correct answer : 60 units

Explanation:

According to the Joint British Diabetes Societies (JBDS) guidelines, it is considered best practice to restart oral or injectable hypoglycaemic postoperatively once the patient is able to eat and drink.

- If the patient has good glycaemic control (HbA1c <7.5%), restart the usual diabetes treatment when a meal is due. Do not stop VRIII until at least 30 minutes after treatment has been given and the patient has eaten.
- If glycaemic control is sub-optimal (HbA1c>7.5%), in addition to the above, the patient may need additional hypoglycaemic therapy such as insulin depending on individualized goals.
- Calculating subcutaneous insulin dose (total daily dose TDD) in insulin-naïve patients, or where an insulin regime needs altering because of sub-optimal control can be done in two possible ways:

  A) Calculating estimated insulin dose from the patient's weight:
  - Frail elderly patients, renal failure (CKD stage 4 or 5), severe hepatic failure, newly diagnosed Type 1 diabetes:

    Total daily insulin dose = 0.3 x bodyweight in kg
  - All other adult patients: Total daily insulin dose = 0.5 x bodyweight in kg

  B) Calculating estimated insulin dose from insulin requirements during the last 6 hours of VRIII as,
  - Divide the total dose of insulin administered in the last 6 hours of the VRIII by 6 to calculate the average hourly dose of insulin.
  - Multiply this by 20 (not 24, to reduce risk of hypoglycaemia) to estimate the patient's total daily insulin requirement. A further correction may be needed in some patients, depending on individual insulin sensitivity, previous degree of glycaemic control and severity of intercurrent illness.

    In this case:

    Insulin in last 6 hours - 18 units

    Divide by 6 – 18/6= 3 units /hour

    Multiply by 20 – 3x20= 60units
  - CBG should be checked one hour after discontinuing VRIII, at least four-hourly for the first 24 hours after VRIII has been discontinued, and between two and four times a day for all in-patients on subcutaneous insulin.

- Adjust the doses of insulin according to blood glucose measurements. A target of 6.0-10.0 mmol/L is appropriate for most in-patients, but patients with significant comorbidities may benefit from less stringent targets (4.0-12.0 mmol/L)

  Reference:

- JBDS-IP (March 2016). Management of adults with diabetes undergoing surgery.
- JBDS-IP (2014). Variable rate insulin infusion (VRII) for medical inpatients with diabetes.

Question 24

A 60-year-old man presented to the emergency department with an altered sensorium for the last 24 hours. He had a history of polyuria and fatigue for the last 5 days. He was a known diabetic with poor medication compliance. On examination, he was confused with a Glasgow Coma Scale of 12/15. He was tachycardic, tachypneic, dehydrated and his blood pressure was found to be 100/60 mmHg. Blood glucose at the time of presentation was 34mmol /L (612mg/dL). Further blood tests revealed:

Test	Result	Normal Range
ABGs	pH7.31	(7.35-7.45)
HCO3	18mEq/L	(22-28)
Urinary ketones	++	
Capillary blood ketone	2mmol/L	(<0.6)
Serum osmolality	330mOsmol/kg	(285-295)

What should be the immediate management (0 to 60 minutes) as per JBDS guidelines, consistent with the underlying diagnosis?

- **A)** Commence insulin infusion at 0.1units/kg/hour
- **B)** Commence IV 0.45% sodium chloride
- **C)** Commence IV 0.9% sodium chloride
- **D)** Commence IV 0.9% sodium chloride and insulin infusion at 0.05units/kg/hour after 60 minutes
- **E)** Commence IV 0.9% sodium chloride with insulin infusion at 0.05units/kg/hour at time zero

Answer

Correct answer : Commence IV 0.9% sodium chloride with insulin infusion at 0.05units/kg/ hour at time zero

Explanation:

The clinical features of raised blood glucose (34mmol/L) and severe hypertonicity (serum osmolality 330mOsmol/kg) along with ketosis (ketonaemia (3ß-hydroxy butyrate greater than 1 mmol/L) or ketonuria 2+ or more) and mild acidosis (pH greater than 7.3, bicarbonate greater than 15 mmol/L) are suggestive of mixed DKA (diabetic ketoacidosis) and HHS (hyperosmolar hyperglycaemic state). According to JBDS guidelines,

Hour 1: Immediate management upon diagnosis: 0 to 60 minutes

T=0 at time intravenous fluids are commenced. If there is a problem with intravenous access critical care support should be requested immediately.

- Commence IV 0.9% sodium chloride – 1 litre to run over 1 hour
  - Consider more rapid replacement if systolic blood pressure is below 90 mmHg
  - Caution in the elderly where too rapid rehydration may precipitate heart failure but insufficient rehydration may fail to reverse acute kidney injury.
  - Use 0.9% sodium chloride solution as the principle fluid to restore circulating volume and reverse dehydration.
  - However, if the osmolality is no longer declining despite adequate fluid replacement with 0.9% sodium chloride solution AND an adequate rate of fall of plasma glucose is not being achieved then 0.45% sodium chloride solution should be substituted.
- Only commence an insulin infusion if there is significant ketonaemia (3ß-hydroxybutyrate greater than 1 mmol/L) or ketonuria 2+ or more (i.e. mixed DKA and HHS). This indicates relative hyperinsulinemia and insulin should be started at time zero.
  - If significant ketonaemia is not present (3ß-hydroxy butyrate is less than 1 mmol/L), do not start insulin.
  - The recommended insulin dose is a fixed rate intravenous insulin infusion (FRIII) given at 0.05 units per kg per hour.
  - A fall of glucose at a rate of up to 5 mmol/L per hour is ideal and once the blood glucose has ceased to fall following initial fluid resuscitation, reassessment of fluid intake and evaluation of renal function must be undertaken. Insulin may be started at this point, or, if already in place, the infusion rate increased by 1 unit/hr.
  - As with DKA, a FRIII is preferred, though generally lower doses are required.

Reference:

- JBDS-IP (August 2012). Management of Hyperosmolar Hyperglycemic State(HHS)

Question 25

A 65-year-old man had been diagnosed with type 2 diabetes at the age of 40 years. Prior to hospital admission, he was prescribed metformin and gliclazide. He was admitted with left-sided hemiparesis and a stroke was diagnosed in the medical assessment unit. A nasogastric tube (NGT) was inserted as his gag reflex was absent and enteral feeding via NGT was commenced, as decided by the multidisciplinary team, at a rate of 75ml/hour with an intended duration of 20 hours/day. A dietician was requested to prescribe an appropriate feed regimen. The patient's blood glucose persistently remained >12mmol/L. In addition to liquid metformin via NGT, premixed (30/70) insulin was recommended at the start and midpoint of the feed. According to JBDS guidelines, what is the total daily insulin dose for a patient receiving enteral feed with a carbohydrate content of 16gm/100ml?

- **A)** 18 units
- **B)** 20 units
- **C)** 22 units
- **D)** 24 units
- **E)** 28 units

Answer

Correct answer : 24 units

Explanation:

All patients who present with acute stroke should have a capillary blood glucose checked on admission to hospital, as hyperglycaemia in stroke patients is common, and associated with worse outcomes. Hyperglyacemia is likely to be encountered if a patient with diabetes is to be fed via the enteral route and controlling hyperglycaemia resulting from enteral feeding will benefit people with diabetes who have had a stroke.

The JBDS guideline recommends glucose targets of 6-12 mmol/l for management of diabetes during enteral feeding and in the pre-feed state, the targets should be 5-8 mmol/l.

Treat if capillary blood glucose is persistently >12 mmol/l.

- Metformin liquid administered via the NGT may be considered for mild hyperglycaemia (e.g. capillary blood glucose up to 12 mmol/l) in people with well controlled type 2 diabetes, or as an adjunct in uncontrolled type 2 diabetes.
- Assess feed regimen and commence an insulin regimen from the choices below:
  - 1. Pre-mixed (30/70) human insulin at start and midpoint of feed.
  - 2.Isophane insulin at start and midpoint of feed.
  - 3.Continuation of basal insulin if already prescribed with bolus doses soluble insulin at start, 6 and 12 hours into feed as required.

    Premixed or isophane is used for feed that are 12-24 hours long. If hyperglycaemia is not controlled with these insulins, start basal as long-acting insulin analogue.
- Calculating the initial insulin dose from carbohydrate content of feed –

  Total humulin dose= [Total carbohydrate intake from feed] divided by [Carbohydrate-to-insulin ratio]
  - a) *Total carbohydrate intake from enteral feed*- That is the total carbohydrate intake expected from the enteral feed over the duration of feed (e.g. 16, 20, 24 hrs). This is calculated as: [Infusion rate (ml/hour)] x [carbohydrate content (g/100 ml)] x [duration of feeding] ÷100
  - b) *Carbohydrate-to-insulin ratio (CIR)*- This is how many grams of carbohydrate/glucose are covered by 1 unit of insulin. The blood glucose rise from enteral feeds is much more than would occur for normal meals: therefore, 1 unit of insulin will cover less of a carbohydrate load.
  - i.If not usually on insulin use a CIR value of 10.
  - ii.If usual Total Daily Insulin Dose (TDID) less than 40 units use a value of 8.
  - iii.If usual Total Daily Insulin Dose (TDID) more than 40 units use a value of 6.

    In this case,

Carbohydrate content of feed (g/100 ml) = 16 Intended infusion rate of enteral feed (ml/hour) = 75 Intended duration of feed (hrs per day) = 20 Not previously on insulin - therefore CIR = 10 Total Humulin 70/30 dose = 16 x 75 x 20 = 24 units/24 hrs 10 x 100

Reference:

- JBDS-IP (Updated July 2012). Glycaemic management during enteral feeding in stroke.

Question 26

A 65-year-old man had been diagnosed with type 2 diabetes at the age of 40 years. Prior to hospital admission, he was prescribed metformin and gliclazide. He was admitted with left-sided hemiparesis and a stroke was diagnosed in the medical assessment unit. A nasogastric tube (NGT) was inserted as his gag reflex was absent and enteral feeding via NGT was commenced, as decided by the multidisciplinary team, at a rate of 75ml/hour with an intended duration of 20 hours/day. A dietician was requested to prescribe an appropriate feed regimen. The patient's blood glucose persistently remained >12mmol/L. In addition to liquid metformin via NGT, premixed (30/70) insulin was recommended at the start and midpoint of the feed. According to JBDS guidelines, what is the total daily insulin dose for a patient receiving enteral feed with a carbohydrate content of 16gm/100ml?

- **A)** 18 units
- **B)** 20 units
- **C)** 22 units
- **D)** 24 units
- **E)** 28 units

Answer

Correct answer : 24 units

Explanation:

All patients who present with acute stroke should have a capillary blood glucose checked on admission to hospital, as hyperglycaemia in stroke patients is common, and associated with worse outcomes. Hyperglyacemia is likely to be encountered if a patient with diabetes is to be fed via the enteral route and controlling hyperglycaemia resulting from enteral feeding will benefit people with diabetes who have had a stroke.

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- Metformin liquid administered via the NGT may be considered for mild hyperglycaemia (e.g. capillary blood glucose up to 12 mmol/l) in people with well controlled type 2 diabetes, or as an adjunct in uncontrolled type 2 diabetes.
- Assess feed regimen and commence an insulin regimen from the choices below:
  - 1. Pre-mixed (30/70) human insulin at start and midpoint of feed.
  - 2.Isophane insulin at start and midpoint of feed.
  - 3.Continuation of basal insulin if already prescribed with bolus doses soluble insulin at start, 6 and 12 hours into feed as required.

    Premixed or isophane is used for feed that are 12-24 hours long. If hyperglycaemia is not controlled with these insulins, start basal as long-acting insulin analogue.
- Calculating the initial insulin dose from carbohydrate content of feed –

  Total humulin dose= [Total carbohydrate intake from feed] divided by [Carbohydrate-to-insulin ratio]
  - a) *Total carbohydrate intake from enteral feed*- That is the total carbohydrate intake expected from the enteral feed over the duration of feed (e.g. 16, 20, 24 hrs). This is calculated as: [Infusion rate (ml/hour)] x [carbohydrate content (g/100 ml)] x [duration of feeding] ÷100
  - b) *Carbohydrate-to-insulin ratio (CIR)*- This is how many grams of carbohydrate/glucose are covered by 1 unit of insulin. The blood glucose rise from enteral feeds is much more than would occur for normal meals: therefore, 1 unit of insulin will cover less of a carbohydrate load.
  - i.If not usually on insulin use a CIR value of 10.
  - ii.If usual Total Daily Insulin Dose (TDID) less than 40 units use a value of 8.
  - iii.If usual Total Daily Insulin Dose (TDID) more than 40 units use a value of 6.

    In this case,

Carbohydrate content of feed (g/100 ml) = 16 Intended infusion rate of enteral feed (ml/hour) = 75 Intended duration of feed (hrs per day) = 20 Not previously on insulin - therefore CIR = 10 Total Humulin 70/30 dose = 16 x 75 x 20 = 24 units/24 hrs 10 x 100

Reference:

- JBDS-IP (Updated July 2012). Glycaemic management during enteral feeding in stroke.

Question 1

A 23 year old female is referred with irregularity of her periods. She takes the combined oral contraceptive microgynon and informs you that her periods are apt to being rather irregular despite compliance with treatment. Menarche was at 12 years of age and her periods were occasionally irregular up until she commenced microgynon two years ago. She went to her GP about the irregular periods, he took some blood tests and found the following which concerns him:

		Normal Ranges
Estradiol	<80 pmol/l	(130-800)
LH	1 mu/l	(2-10)
FSH	1 mu/l	(2-10)
Prolactin	388 mu/l	(50-450)
TFTs	Normal	

Which of the following is the most likely explanation for her results?

- **A)** Drug induced
- **B)** Kallmann syndrome
- **C)** Pituitary macroadenoma
- **D)** Polycystic ovarian syndrome
- **E)** Turner's mosaic

Answer

Correct answer : Drug induced

This patient takes the OCP – microgynon. This contains ethinyl-oestradiol which is a synthetic oestrogen that is not detected on conventional 17 beta-oestradiol assays. The OCP is designed to suppress LH/FSH, production of endogenous oestradiol and hence ovulation. One should not check estradiol/LH/FSH when the patient is receiving the OCP.

Question 2

A 25 year old male presents with reduced libido and erectile dysfunction. There is nil of note on examination and his visual fields reveal a bitemporal constriction of his visual fields. Visual acuity is 6/9 in both eyes and fundoscopy reveals no abnormality. His investigations reveal:

		Normal Ranges
LH	1.1 mu/l	(2 - 100)
FSH	2.0 mu/l	(2 - 10)
Testosterone	6.2 nmol/l	(8 - 30)
Prolactin	38,000 mu/l	(<450)

MRI reveals a 3 cm pituitary macroadenoma that displaces the optic chiasm.
Which of the following is the most appropriate management of this patient?

- **A)** Commence cabergoline
- **B)** Refer for pituitary radiotherapy
- **C)** Refer for pituitary surgery
- **D)** Treat with testosterone only and repeat MRI in 3 months
- **E)** Treat with somatostatin analogue

Answer

Correct answer : Commence cabergoline

This patient has a macroprolactinoma and presented with features of hypogonadism. His MRI reveals that the tumour is pressing on the optic chiasm and there is a bitemporal visual field defect. Even so, dopamine agonist therapy would be the treatment of choice for this macroprolactinoma. The tumour would be expected to shrink rapidly with treatment and the visual fields to open up. Surgery is rarely required for prolactinomas and is reserved for dopamine agonist resistance or intolerance. Repeating the MRI in approximately 3 months would be expected to reveal the abrupt reduction in volume and suppression of prolactin concentrations.

https://emedicine.medscape.com/article/124634-treatment

Question 3

A 33 year old female presents with deteriorating hirsutism and amenorrhoea. Menarche had been at the age of 12 and periods had generally been irregular. She has two children aged 8 and 6 but has noted a deterioration of facial hirsutism over the last 2-3 years. Investigations reveal:

		Normal Ranges
Estradiol	450 pmol/l	(130 - 800)
LH	8.8 mu/l	(2 - 10)
FSH	2.8 mu/l	(2 - 10)
Testosterone	3.3 mu/l	(<3)
Prolactin	380 mu/l	(<450)
Androstenedione	16.6 pmol/l	(2 - 10)

What is the most likely diagnosis?

- **A)** Adrenal tumour
- **B)** Cushing's disease
- **C)** Non-classical congenital adrenal hyperplasia
- **D)** Ovarian tumour
- **E)** Polycystic ovarian syndrome

Answer

Correct answer : Polycystic ovarian syndrome

The most likely diagnosis in this patient with a long history of menstrual irregularity, hirsutism and mild hyperandrogenism ispolycystic ovarian syndrome (PCOS). An adrenal or ovarian tumour is most unlikely and one should investigate for a possible tumour with a testosterone above 5. The high androstenedione is again compatible and suggestive of PCOS.

Question 4

A 55 year old female presents with deteriorating hirsutism of 10 months duration together with a six month history of amenorrhoea. Examination reveals quite marked facial hirsutism around the jawline and moustache region as well as hair on the arms and extending from the pubis to the umbilicus. Her investigations reveal:

		Normal Ranges
Estradiol	80 pmol/l	(<130)
LH	18.2 mu/l	(2 - 10)
FSH	38 mu/l	(2 - 10)
Testosterone	15.5 nmol/l	(<3)

Which of the following is the most appropriate investigation for this patient?

- **A)** 1mg overnight dexamethasone test
- **B)** 17-hydroxyprogesterone concentration
- **C)** 24hr urine free cortisol
- **D)** CT abdomen/pelvis
- **E)** Transvaginal ovarian ultrasound

Answer

Correct answer : CT abdomen/pelvis

One needs to suspect a tumour (either ovarian or adrenal) in this patient from the rapidity of the development of postmenopausal hirsutism to the very high testosterone concentration. Generally, a testosterone concentration >5 nmol/l merits further evaluation for a potential testosterone secreting tumour and levels above 8 do suggest a virlising tumour such as an adrenal tumour or hyperthecosis. Thus CT of the abdomen would be the most appropriate investigation.

Investigation of androgen excess

Question 5

A 26 year old male with a history of treated childhood craniopharyngioma and associated hypopituitarism wishes to discuss fertility. He has confirmed panhypopituitarism and receives hydrocortisone, thyroxine, growth hormone and testosterone for hypopituitarism but now wishes to commence a family. On examination of the genitalia, his testicular volumes are approximately 10 mls bilaterally and he has normal secondary sexual characteristics. A semen analysis after stopping testosterone reveals azoospermia and his plasma testosterone is also low. Which of the following would be the most appropriate treatment for this man?

- **A)** Advise sperm donation
- **B)** Continue testosterone in current dose
- **C)** Stop testosterone and commence HCG injections
- **D)** Stop testosterone, GH and commence HCG injections
- **E)** Refer for intracytoplasmic sperm injection (ICSI)

Answer

Correct answer : Stop testosterone and commence HCG injections

The patient has hypogonadotropic hypogonadism and needs assisted fertility. The most appropriate approach would be treatment with human chorionic gonadotropin (HCG) injections aiming to firstly restore testosterone concentrations and hopefully generate semen production although one might need to add ollicle-stimulating hormone (FSH) if testosterone is restored yet azoospermia persists. If HCG is unsuccessful then the patient may need referral for intracytoplasmic sperm injection (ICSI) or alternatively may wish to consider sperm donation.

Question 6

A 24 year old female with a diagnosis of polycystic ovarian syndrome is keen to start a family. She was diagnosed with PCOs at the endocrine clinic following presentation with oligomenorrhoea and mild hirsuties. She is overweight with a BMI of 27 kg/m^2 and she has a menstrual cycle of approximately 6-8 weeks. She has been trying for the last year to conceive but has been unsuccessful. Her partner has had semen analysis performed by the GP which is normal. Investigations reveal:

		Normal Ranges
Estradiol	450 pmol/l	(130 - 800)
LH	8.3 mu/l (2 - 10)	
FSH	2.2 mu/l	(2 - 10)
Testosterone	2.2 pmol/l	(<3)
Prolactin	380 mu/l	(<450)

Which of the following would be the most appropriate approach to treating this patient?

- **A)** Bromocriptine
- **B)** Clomiphene
- **C)** Continue with no treatment
- **D)** Metformin
- **E)** Requires IVF

Answer

Correct answer : Clomiphene

This woman has subfertility, as infertility is considered as 2 years or more unprotected intercourse without conception. In this case, the most appropriate initial treatment would be clomiphene as suggested by a study in the NEJM 2007. Conception rates were 22.5% with clomiphene vs 7% with metformin. If this fails then the addition of metformin to the clomiphene may improve chances still further.

Question 7

A 32 year old female who has been treated with cabergoline for a microprolactinoma attends clinic and informs you that she is 8 weeks pregnant. She has been continuing to take the cabergoline 0.25 mg twice weekly and the pregnancy was unexpected but she would like to continue with the pregnancy. Which of the following would you advise?

- **A)** Advise termination due to the teratogenic risk with cabergoline
- **B)** Continue cabergoline at current dose
- **C)** Increase dose of cabergoline
- **D)** Stop cabergoline
- **E)** Switch cabergoline to bromocriptine

Answer

Correct answer : Stop cabergoline

Pregnancy on patients taking dopamine agonist therapy for prolactin secreting tumours is not uncommon and there is no evidence that taking these agents is harmful to the fetus. However, there is no need to take these agents during pregnancy as the risks of tumour expansion are small (<1%). Thus, the patient should be advised to stop cabergoline only.

Question 8

A 26 year old female with a microprolactinoma falls pregnant after taking cabergoline. She is advised to stop the cabergoline.

How would you continue to serially monitor the patient during her pregnancy?

- **A)** Clinical observation
- **B)** Formal visual field assessment
- **C)** MRI pituitary every trimester
- **D)** Prolactin concentrations
- **E)** Short synacthen tests

Answer

Correct answer : Clinical observation

The prolactin concentration rises in normal pregnancy and is typically in the thousands. There is no need to measure prolactin concentrations during pregnancy. There is a small risk of tumour expansion during pregnancy (less than 1%) and so the patient should be monitored clinically with clinical field assessment and if there is a suspicion of tumour expansion then MRI can be undertaken.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4443771/

Question 9

A 55 year old male is referred for problematic erectile dysfunction with sildenafil. He has a 8 year history of type 2 diabetes for which he takes metformin 500 mg tds and has a HbA1c of 52 mmol/mol. He has tried sildenafil in escalating doses over the last three months taking 100mg on the last 10 attempts at intercourse but feels that this has not produced an adequate erection enabling penetrative sex. His investigations show:

		Normal Ranges
Testosterone	13.2 nmol/l	(9 - 30)
LH	3.6 mu/l	(2 - 10)
FSH	4.5 mu/l	(2 - 10)

Which of the following would be the most appropriate treatment for this man?

- **A)** Intracavernosal injection of alprostadil
- **B)** Surgical insertion of an intracavernosal pump
- **C)** Tadalafil
- **D)** Testosterone gel
- **E)** Vacuum pump device

Answer

Correct answer : Intracavernosal injection of alprostadil

Approximately 20% of patients fail PDE-5 inhibitors such as sildenafil/tadalafil. It is important to ensure that testosterone concentrations are normal if one is to secure the adequacy of PDE-5 inhibitor therapy. In this case, the testosterone concentration is adequate. Under these circumstances, the most appropriate treatment would be intracavernosal injections with alprostadil – caverject. The patient should be shown how to draw up, dose and inject the alprostadil and to seek medical advice should priapism develop.

Guidelines on the management of ED

Question 10

A 48 year old male presents with a history of reduced libido and erectile dysfunction. His GP encloses the following results:

		Normal Ranges
Testosterone	7.1 nmol/l	(9 - 30)
LH	2.2 mu/l	(2 - 10)
FSH	3.6 mu/l	(2 - 10)

He informs you that he has two children who are grown up, he drinks approximately 10 units of alcohol weekly and he has noticed that the development of erectile dysfunction has occurred over a few years.

On examination he has a BMI of 37.5 kg/m^2, a blood pressure of 136/88 mmHg and a pulse of 68 bpm. No abnormalities are found in cardiovascular, chest or abdominal examination.
Further results are obtained which reveal:

U+Es	Normal
Fasting Plasma Glucose	6.1 mmol/l
Free T4	12.1 pmol/l (9- 22)
TSH	3.2 mu/l (0.5 - 5)
Prolactin	230 mu/l (50 - 450)

A CT head scan is performed which reveals no abnormality of the pituitary.
Which of the following is the most likely cause for his hypogonadism?

- **A)** Haemochromatosis
- **B)** Kallmann syndrome
- **C)** Obesity
- **D)** Pituitary microadenoma
- **E)** Testicular fibrosis

Answer

Correct answer : Obesity

This patient's results reveal a low testosterone with 'inappropriately' normal LH and FSH indicating a hypogonadotropic hypogonadism. His other pituitary function is normal and his CT of the pituitary is also reported as normal. However, he is obese and has features of the metabolic syndrome with an elevated fasting plasma glucose. With these results, the most probable cause of his hypogonadism is obesity.

This is a well described phenomena and the exact cause is ill-understood although is believed to directly relate to visceral fat mass with increasing aromatisation of testosterone to oestradiol and then feedback on the Pituitary.

Question 11

A 22 year old female presents with a long history of oligomenorrhoea, weight gain and hirsutism. Elevation of which of the following would be most suggestive of a diagnosis of polycystic ovarian syndrome?

- **A)** Androstenedione
- **B)** DHEAS
- **C)** Insulin
- **D)** LH:FSH ratio
- **E)** Prolactin

Answer

Correct answer : Androstenedione

Androstenedione, a weak androgen produced in the ovaries is typically elevated in PCOS. Although, prolactin is elevated in approx 10% of patients with PCOs with concentrations typically less than 1000 mu/l, higher concentrations may prompt investigation for prolactinoma. Although insulin resistance is a feature of PCOs, its concentration, per se, is rather meaningless in PCOs. Only about 30% of patients with PCOs have elevated LH:FSH ratio and about the same have a modestly elevated testosterone. However 80% will have elevation of androstenedione, a weak androgen synthesised in the ovaries.

PCOS

Question 12

A 32 year old female with a diagnosis of polycystic ovarian syndrome is referred to the endocrine clinic. She has a history of weight gain and modest facial hirsuties. Her periods are reasonably irregular occurring once every two-three months. She is keen to commence a family and has had unprotected sex for at least three years without conception. Investigations reveal:

		Normal Ranges
Estradiol	420 pmol/l	(130 - 800)
LH	8.8 iu/l	(3 - 10)
FSH	2.2 iu/l	(3 - 10)
Prolactin	580 mu/l	(50 - 500)
TFTs	Normal	

Which of the following would be the most appropriate agent for this patient?

- **A)** Bromocriptine
- **B)** Cabergoline
- **C)** Metformin
- **D)** Spironolactone
- **E)** Yasmin - combined OCP with drospirenone

Answer

Correct answer : Metformin

This patient has the features of PCOs and the modest elevation of prolactin is quite typical of this condition occurring in approximately 10% of cases. In this case, the hyperprolactinemia appears not to be pathological as the estradiol is normal. Metformin would be the most appropriate treatment of all the options to reduce the insulin resistance. Metformin may regulate menstrual periods by improving ovulatory function. However, the effect on live birth rate has not been established. Spironolactone should not be used in patients wishing to conceive as it is teratogenic. This woman wants to get pregnant so the combined OCP is counter intuitive.

RCOG paper Metformin and Fertility

Question 13

A 25 year old female presents with problematical facial hirsutism. All investigations support a diagnosis of polycystic ovarian syndrome. You decide to prescribe eflornithine cream. Which of the following describes its mechanism of action?

- **A)** 5-alpha reductase inhibitor
- **B)** Dihydrotestosterone receptor antagonist
- **C)** Insulin sensitiser
- **D)** Lipase inhibitor
- **E)** Ornithine decarboxylase inhibitor

Answer

Correct answer : Ornithine decarboxylase inhibitor

Eflornithine is an ornithine decarboxylase inhibitor and interferes with the urea cycle important in hair growth. It is used in the treatment of hirsutism and is associated with significant improvement in cosmetic appearance.

Question 14

A 55 year old male presents with problems with erectile function. He has a poor libido and denies any early morning erections. He has fathered two children and his current problems date over the last two years. On examination, he appears a phenotypically normal male, has a BMI of 38 kg/m^2 and has normal male distribution of body hair. Testicular examination reveals testes of 12-15 mls bilaterally.
Investigations reveal:

		Normal Ranges
Fasting Plasma Glucose	6.1 mmol/l	(3.5-5.5)
Testosterone	6.6 nmol/l	(9-30)
LH	2.8 iu/l	(3-10)
FSH	3.4 iu/l	(3-10)
Prolactin	410 mu/l	(<450)
Free T4	12.8 pmol/l	(9-23)
TSH	3.2 mu/l	(0.5-5)

Which of the following is likely to explain this man’s results?

- **A)** Craniopharyngioma
- **B)** Haemochromatosis
- **C)** Kallmann syndrome
- **D)** Non-functional pituitary tumour
- **E)** Obesity

Answer

Correct answer : Obesity

The most likely cause of this man’s hypogonadotropic hypogonadism is obesity. Increasingly, obesity is being recognised as a cause of hypogonadism although the mechanism is somewhat obscure. The other options which cause hypogonadotropic hypogonadism are listed but these are less likely although one would undertake pituitary imaging.

Question 15

A 15-year-old female with increasing obesity was referred to the clinic with abdominal swelling and mild ankle oedema. On examination, the blood pressure was 142/88 mmHg.
Investigations reveal:
< />

		Normal Ranges
Haemoglobin	10.5 g/dL	(11.5-16.5)
Serum biochemistry	Normal	
Serum albumin	34 g/L	(37-49)
Urine dipstick	Proteinuria +	

Which of the following is the most appropriate investigation for this patient?

- **A)** 24 hour urinary protein estimation
- **B)** Abdominal ultrasound
- **C)** Protein electrophoresis
- **D)** Urinary albumin: creatinine ratio
- **E)** Urinary B-human chorionic gonadotrophin test (B-HCG)

Answer

Correct answer : Urinary B-human chorionic gonadotrophin test (B-HCG)

This young girl has 'gained weight' with abdominal swelling and ankle oedema. She is hypertensive, has proteinuria and is anemic. This should raise a suggestion of a concealed pregnancy with pre-eclampsia. The most relevant investigation would be a pregnancy test - urinary B-HCG.

Question 16

A 72 year old male is referred by his GP who was concerned about an elevated prolactin concentration. He had been well up until 3 years ago when he was diagnosed with prostate cancer and was treated with GnRH analogues. Since then he has been tired but his prostate cancer is well controlled, being on 6 monthly appointments with urology. His GP had checked a few results and found that his prolactin was 980 mu/l (50-450), precipitating referral. He currently receives amlodipine, ramipril, simvastatin and domperidone

He appears hypogonadal in appearance and his blood pressure is 134/74 mmHg with a BMI of 32 kg/m^2.

Investigations reveal:

		Normal Ranges
Testosterone	1.2 nmol/l	(8-30)
Prolactin	800 mu/l	(50-450)
LH	1.2 mu/l	(1-10)
FSH	1.1 mu/l	(1-10)
Free T4	9.1 nmol/l	(9-23)
TSH	4mu/l	(0.5-5)
IGF-1	18 nmol/l	(15-30)

Which of the following is the likely cause for the hyperprolactinemia?

- **A)** Drug induced
- **B)** Metastatic prostatic disease
- **C)** Microprolactinoma
- **D)** Non-functioning pituitary tumour
- **E)** Primary hypothyroidism

Answer

Correct answer : Drug induced

This patient is receiving a dopamine antagonist - domperidone. This is the most likely cause for his hyperprolactinemia. The thyroid function tests are entirely normal and a microprolactinoma would be very unusual in a man of this age. The suppression of LH, FSH and testosterone indicates adequate treatment with GnRH analogues.

Question 17

A 25 year old man has been referred to the fertility clinic for routine assessment. He has been in a steady relationship for the last 2 years but his partner has been unable to conceive despite unprotected sexual intercourse between the couple for more than 1 year.

His partner has been thoroughly investigated with no obvious physical or hormonal abnormality noticed in her as a cause for infertility.

He is otherwise asymptomatic, with no significant past medical history and denies usage of any illicit substance. Physical examination performed in clinic is normal, with normal secondary sexual characteristics and testicular volume of 15 mls bilaterally.

What's the first investigation you would offer to him for further analysis of any male factor involved in infertility?

- **A)** Follicle stimulating hormone (FSH)/luteinizing hormone (LH)
- **B)** Karyotyping
- **C)** Semen analysis
- **D)** Testosterone levels
- **E)** Thyroid function test (TFT)

Answer

Correct answer : Semen analysis

Infertility is defined as the failure to conceive despite 2 years of unprotected sexual intercourse. Investigations are warranted if the couple fails to conceive despite 1 year of unprotected intercourse. One third of the causes of infertility are related to male factor. The commonest of male factor infertility causes include primary gonadal failure, secondary gonadal failure, genital tract abnormalities, erectile dysfunction, systemic illness or iatrogenic due to drugs such as steroids, antiandrogens, spironolactone etc. Primary gonadal failure is commonly due to genetic syndromes like Klinefelter syndrome or orchitis, testicular torsion, mumps or congenital cryptorchidism. While secondary gonadal failure is most commonly due to pituitary or hypothalamic disease.

The investigations for male factor infertility include semen analysis, which if normal practically rules out any male factor contributing to infertility. Other investigations include measurement of FSH, LH and testosterone levels to categorise patients into primary or secondary gonadal failure.

Question 18

A 24 year old gentleman, presents to the endocrine clinic for further assessment regarding azoospermia, noted on investigation of infertility. He is 182 cm tall with a bodyweight of 70 Kg and body bass index (BMI) of 21kg/m^2. On examination, he has bilateral gynaecomastia and testicular volume of 6 ml with testes being firm in consistency. His investigations are shown below:

		Normal Ranges
FH	28 U/L	(1.4-18.1)
LH	42 U/L	(3.0-8.0)
Prolactin	110 mU/L	(45-375)
Testosterone	4.2 nmol/L	(8.4-28.7)
Free T_4	18 pmol/L	(11.5-22.7)
TSH	1.6 mU/L	(0.35-5.5)

What is the most appropriate next step for the management of his infertility?

- **A)** Cabergoline
- **B)** Gonadotrophin-releasing hormone (GnRH) analogue therapy
- **C)** Growth Hormone treatment
- **D)** Refer to fertility clinic for evaluation
- **E)** Testosterone replacement

Answer

Correct answer : Refer to fertility clinic for evaluation

This gentleman has primary gonadal failure based on his low testosterone levels and increased FSH/ LH levels. His tall stature, bilateral gynaecomastia and small testicular volume point towards testosterone deficiency developing before he attained puberty, leading to eunuchoid physical appearance. It is likely that he suffers from a genetic disorder like Klinefelter`s syndrome and will need further karyotype analysis to establish the diagnosis. These patients require lifelong replacement with testosterone and are infertile. In contrast to secondary hypogonadism which can be treated with pulsatile GnRH treatment, the management of infertility in primary hypogonadism usually requires modalities like in vitro fertilisation (IVF) or intra cytoplasmic sperm injection (ICSI) and better achieved under specialist fertility clinic care.

Question 19

A 16 year girl presents to the clinic with primary amenorrhoea. She has Tanner stage 4 breast development but scanty axillary and pubic hair. The only past medical history of note is an inguinal hernial repair at the age of 6. Which of the following is the next best investigation to establish her diagnosis?

- **A)** Follicle stimulating hormone (FSH)/luteinizing hormone (LH)/estradiol levels
- **B)** mutation analysis
- **C)** Pelvic ultrasound
- **D)** Pregnancy test
- **E)** 17 Hydroxyprogesterone levels (17 OHP)

Answer

Correct answer : mutation analysis

This 16 year old has complete androgen insensitivity syndrome as suggested by the presence of primary amenorrhoea, scanty hair growth and a history of a previous inguinal hernial repair pointing towards the previous presence of ectopic testicular tissue. It is an X linked recessive disorder due to a mutation of the androgen receptor gene located on Xq11-12, although a negative family history may be present in more than one third cases.

The diagnosis is usually suspected based on a clinical profile including primary amenorrhoea, normal breast development, lack of axillary and pubic hair and testis like masses in the inguinal canal or labia. The testosterone levels are clearly higher than the normal female range and oestrogen levels are low. LH levels are elevated with normal FSH levels. The management includes affirmation and reinforcement of female gender identity and removal of testicular tissue (orchidectomy) after attaining puberty so as to avoid development of any malignancy in the ectopic gonadal tissue.

Question 20

A 16 year girl presents to the clinic with primary amenorrhoea. She has Tanner stage 4 breast development but scanty axillary and pubic hair. The only past medical history of note is an inguinal hernial repair at the age of 16. What is the likely diagnosis?

- **A)** Androgen insensitivity syndrome
- **B)** CAH
- **C)** Gonadal dysgenesis
- **D)** PCOS
- **E)** Turner`s syndrome

Answer

Correct answer : Androgen insensitivity syndrome

This 16 year old has complete androgen insensitivity syndrome as suggested by the presence of primary amenorrhoea, scanty hair growth and a history of a previous inguinal hernial repair pointing towards the previous presence of ectopic testicular tissue. It is an X linked recessive disorder due to a mutation of the androgen receptor gene located on Xq11-12, although a negative family history may be present in more than one third cases.

The diagnosis is usually suspected based on a clinical profile including primary amenorrhoea, normal breast development, lack of axillary and pubic hair and testis like masses in the inguinal canal or labia. The testosterone levels are clearly higher than the normal female range and oestrogen levels are low. LH levels are elevated with normal FSH levels. The management includes affirmation and reinforcement of female gender identity and removal of testicular tissue (orchidectomy) after attaining puberty so as to avoid development of any malignancy in the ectopic gonadal tissue.

Question 21

A 22 year lady presents with primary amenorrhoea. Her hormonal profiles as checked in the endocrinology clinic are shown below:

		Normal Ranges
FSH	8 U/L	(Follicular 0.5-5, Mid-cycle 8-33, Luteal 2-8 U/L)
LH	60 U/L	(Follicular 3-12, Mid-cycle 20-80, Luteal 3-16 U/L)
Oestradiol	25 pmol/L	(Follicular 17-260, Luteal 180-1100 pmol/L)
Prolactin	160 mU/L	(60-620)
Free T_4	17.2 pmol/L	(11.5-22.7)
TSH	1.1 mU/L	(0.35-5.5)

Her further investigations include an ultrasound of the pelvis which shows a small rudimentary uterus. On karyotyping, a XY mosaic chromosomal pattern is seen. Which is the next crucial step in her long term management?

- **A)** Cabergoline
- **B)** HCG treatment
- **C)** Gonadectomy
- **D)** Combined female HRT
- **E)** Transdermal oestrogen replacement

Answer

Correct answer : Gonadectomy

This lady has primary gonadal failure secondary to gonadal dysgenesis with XY mosaic pattern on karyotype analysis. The XY gonadal dysgenesis can be complete or incomplete. Patients with the complete form present with no phenotypic features of Turner syndrome, with normal or tall stature, female external genitalia, bilateral streak gonads and sexual infantilism. The incomplete form presents with a variable degree of ambiguity in external female genitalia development. There is an increased risk of malignancy associated with dysgenetic gonads and as a result prophylactic gonadectomy should be considered in all cases.

Question 22

A 17 year old girl diagnosed to have Turner's syndrome has completed 2 years of growth hormone (GH) therapy and attained her final height. What should be the next step as far as her GH replacement therapy is concerned?

- **A)** Continue GH therapy indefinitely
- **B)** Half the dose of GH therapy
- **C)** Need to continue GH therapy until she is 25
- **D)** Reassess her GH axis
- **E)** Stop GH therapy

Answer

Correct answer : Stop GH therapy

Therapy in Turner's syndrome is aimed towards induction of secondary sexual characteristics and attainment of maximum possible final height. Growth hormone replacement forms the mainstay of treatment for the later purpose and given at a dose of 45-50 μg/ kg daily for a period of 3-7 years. It is contraindicated if there is presence of any active malignancy, post renal transplant for at least one year or if there is evidence of epiphyseal fusion. GH treatment is discontinued on attainment of final height or if the response is poor (an increase in growth velocity of less than 50% from baseline) in the first year of treatment.

Question 23

A 17 year old girl presents with delayed puberty (Tanner stage 2, breast and hair development), she is also hypertensive and has hypokalaemia. What is the likely underlying enzymatic defect?

- **A)** 3ß HSD
- **B)** 11ß HSD
- **C)** 11ß Hydroxylase
- **D)** 17a hydroxylase
- **E)** 21a hydroxylase

Answer

Correct answer : 17a hydroxylase

Aldosterone and deoxycorticosterone (DOC) are the two most important mineralocorticoid hormones. Aldosterone binding weakly with corticosteroid binding globulin (CBG) and mostly circulates bound to albumin. In contrast 11-Deoxycortisol (DOC) is highly bound to CBG and is usually undetectable in urine. Both of these have equal affinity for the mineralocorticoid receptor but the former is more important as a mineralocorticoid hormone due to its presence in circulation in the free state. Nevertheless, excess DOC secretion, as seen in congenital adrenal hyperplasia (CAH), is associated with hypertension, hypokalaemia and suppression of plasma renin activity and serum aldosterone levels.

In CAH, excessive DOC production is seen with deficiency of either 11ß hydroxylase deficiency or 17a hydroxylase deficiency. The later is associated with decreased production of androgens in addition to the defective synthesis of cortisol. As a result affected males present with features of pseudo-hermaphroditism and affected females present with primary amenorrhoea and features of sexual infantilism.

Question 24

A 21 year old girl with a long standing history of menstrual irregularities presents to her GP with breast tenderness and a 2 month history of amenorrhoea. She has a BMI of 31 kg/m2 and features of hirsutism on examination. What single test will you advise her GP to perform before she is referred to endocrinology clinic?

- **A)** 17 OH Progesterone levels
- **B)** DHEAS
- **C)** Prolactin
- **D)** Testosterone
- **E)** Urinary pregnancy test

Answer

Correct answer : Urinary pregnancy test

It is imperative that pregnancy is ruled out in a female (in the reproductive age group), presenting with secondary amenorrhoea to avoid unnecessary investigations and wastage of resources. Further investigations (for example - FSH, LH, Prolactin, TFT) are only warranted if the initial urinary pregnancy test is negative

Question 25

A 23 year old man, of muscular build, presents to the clinic with reduced libido. He visits the gym regularly and denies usage of any substance of abuse. His BMI is 30 kg/m^2 and he displays normal secondary sexual characteristic development with some acne on his back. His blood results are as shown below:

		Normal Ranges
FSH	1.8 U/L	(1-10)
LH	3.2 U/L	(3-10)
Testosterone	8.1 nmol/L	(9-28.5)
Prolactin	220 mU/L	(45-400)
LFT	normal	
MRI Brain	normal	

What is the likely cause for his hypogonadism?

- **A)** Anabolic steroid abuse
- **B)** Kallmann syndrome
- **C)** Klinefelter's syndrome
- **D)** Idiopathic hypogonadotropic hypogonadism
- **E)** Weight related hypogonadotropic hypogonadism

Answer

Correct answer : Anabolic steroid abuse

This gentleman has secondary hypogonadism as reflected by low testosterone, low FSH and LH levels. His normal secondary sexual characteristic development makes the diagnosis of a genetic disorder unlikely. A normal MRI rules out any structural lesion involving the pituitary gland or hypothalamus. Anabolic steroid abuse is quite common in bodybuilders and sportsmen. The increased aromatase activity in such cases leads to increased conversion of testosterone to oestrogens as a result gonadotropin secretion is suppressed.

The following is a list of major causes of secondary hypogonadism:

- Genetic disorders such as Kallmann syndrome, DAX-1 mutation
- Structural disorders of the pituitary and/or hypothalamus (pituitary adenoma, craniopharyngioma, germinoma)
- Post surgical (pituitary and/or hypothalamic) or post cranial radiotherapy
- Functional - secondary to excessive exercise (e.g. long distance runners), systemic illness, obesity, anorexia, stress, anabolic steroids, recreational drugs
- Infiltrative disease like sarcoidosis, haemochromatosis
- Congenital syndromes like Laurence-Moon-Biedl or Prader-Willi syndrome

Question 26

A 22 year old lady, planning for a family in the near future, has been diagnosed as having a microprolactinoma based on raised prolactin levels and MRI scan results. Which is the best management option in her case?

- **A)** Bromocriptine
- **B)** Cabergoline
- **C)** Observe
- **D)** Radiotherapy
- **E)** Removal of tumour

Answer

Correct answer : Bromocriptine

Bromocriptine is a safe option for females in the reproductive age group presenting with a microprolactinoma if they are seeking a family in the near future. The therapy can be stopped once the patient conceives and pregnancy is confirmed. The dopamine agonists help reduce prolactin levels and induce ovulation. Therefore, if pregnancy is desired women should be given advice regarding contraception on initiation of therapy. Cabergoline usage in pregnant women has also not been associated with any increased risk of foetal malformation, but the available data on its safety profile is limited.
https://bnf.nice.org.uk/drug/bromocriptine.html

Question 27

A 60-year-old man presents with a 1 year history of poor erectile function. He denies any early morning erections, although he feels that his libido is fine. He has a history of hypertension and type 2 diabetes for which he takes amlodipine 5 mg daily, losartan 50 mg daily, simvastatin 40 mg daily and metformin 500 mg tds. He is a smoker of 5 cigarettes daily, drinks 18 units of alcohol weekly and is employed as a taxi driver. He has a stable relationship with his wife and, although she is supportive, he feels that the erectile dysfunction is causing problems with his self-esteem and their relationship.

He has a BMI of 36.5kg/m^2, a blood pressure of 132/82 mmHg and a waist circumference of 105cm. His results reveal:

		Normal Ranges
Testosterone	13 nmol/l	(9-30)
HbA1c	56 mmol/mol (7.3%)	(<42; 6%)
Total cholesterol	4.5 mmol/l	(<5)

Which of the following would be the most appropriate approach to this patient?

- **A)** Arrange cardiovascular assessment
- **B)** Arrange endocrine investigation
- **C)** Commence a PDE-5 inhibitor
- **D)** Commence intracavernosal alprostadil
- **E)** Trial of transdermal testosterone

Answer

Correct answer : Arrange cardiovascular assessment

This patient presents with erectile dysfunction but it needs to be appreciated that this can be representative as an early marker of underlying coronary artery disease. This patient has a number of coronary risk factors including hypertension, dyslipidemia (which is being treated with a statin), smoking, obesity with central adiposity and diabetes. Certainly, this presentation gives the clinician the opportunity to address the vascular risk factors but in this case, guidance suggests that the patient should be further investigated for cardiovascular risk prior to considering any treatment for his erectile dysfunction (1). Although cardiovascular events are rare during sexual activity, the patient should be advised to abstain from sex until investigations such as exercise testing are completed and cardiac risk confirmed. Similarly no treatment should be offered until cardiac status has been properly assessed. Hackett G, Kirby M, Wylie K, et al. British Society for Sexual Medicine Guidelines on the Management of Erectile Dysfunction in Men—2017. J Sex Med 2018;XX:XXXeXXX

Question 28

A 31-year-old man was referred to clinic with infertility and azoospermia. The GP had investigated him and found the following results.

		Normal Ranges
Testosterone	15.5 nmol/l	(9-30)
LH	3.3 mu/l	(1-10)
FSH	30 mu/l	(1-10)
Semen analysis	azoospermia	
Karyotype	46 XY	
PRL/TFTs	Normal	

He had been trying for children for 3 years without success. He gave no previous history of illness and had normal puberty at the age of 13. There was nil of note on abdominal examination and testicular examination was normal with testicular volumes of 15 mls bilaterally. An ultrasound of the testes revealed no specific abnormality and a testicular biopsy performed privately had shown ‘no germ cells with the seminiferous tubules lined by Sertoli cells’.
Which of the following is the likely diagnosis?

- **A)** Fragile X syndrome
- **B)** Kallmann syndrome
- **C)** Klinefelter’s mosaic
- **D)** Leydig cell hyperplasia
- **E)** Sertoli-cell only syndrome

Answer

Correct answer : Sertoli-cell only syndrome

This is a case of Sertoli cell only syndrome which is found in up to 10% of men with azoospermia/oligospermia. The condition may be idiopathic, as suggested in this case, or can occur as a consequence of chromosomal abnormalities such as Klinefelter, viral orchitis (mumps), chemotherapy and radiotherapy.

Sertoli-Cell-Only Syndrome Updated: Apr 17, 2015 Author: Edward David Kim, MD, FACS; Chief Editor: Bradley Fields Schwartz

Question 29

A 65-year-old man is being seen regarding erectile dysfunction. He has previously been seen and diagnosed with late-onset hypogonadism associated with obesity. He has received three months of treatment with a testosterone gel formulation and currently uses 60 mg daily. His most recent result reveals:

		Normal Ranges
Testosterone	18.1 nmol/l	(9-30)

He has noticed an improvement in his energy levels and vitality as well as improved libido, but despite these improvements, his erectile dysfunction persists.
Which of the following would the most appropriate approach to his further management?

- **A)** Add intracavernosal alprostidil (Caverject)
- **B)** Add intraurethral alprostidil (Muse)
- **C)** Add PDE-5 inhibitor
- **D)** Titrate the dose of testosterone to 70mg daily
- **E)** Switch testosterone to intramuscular testosterone

Answer

Correct answer : Add PDE-5 inhibitor

This man has been treated for weight related hypogonadism and is receiving an adequate replacement dose of testosterone, as reflected by the normal testosterone concentration. Despite this, his erectile dysfunction persists and the most appropriate first line approach would be to try a PDE-5 inhibitor such as sildenafil, tadalafil or vardenafil. Success rates of up to 80% with appropriate use of PDE-5 inhibitors may be expected (1).

BSSM Guidelines

Question 30

A 48-year-old man presents to the clinic complaining of increasing erectile dysfunction which has deteriorated over the last 2-3 years. He has also noticed a subtle curvature in the penis. On examination of the flaccid penis, you note that there is a 1.5 cm non-tender, fibrous nodule on the right dorsal aspect of the penis. He is not overly perturbed regarding the curvature of his penis and when he does have an erection, he is able to have penetrative sex. However, over the last 3 years he has found problems with poorly sustained erections. He is otherwise a fit man and takes no medication. His BMI is 28.2 kg/m^2.
His results reveal:

		Normal Ranges
Testosterone	13.3 nmol/l	(9-30)
Glucose	5.1 mmol/l	(3.5-5.5)

Which of the following is the most appropriate approach to the management of this man?

- **A)** Refer for consideration of surgical correction of penis
- **B)** Refer for penile prosthesis
- **C)** Treat with intracavernosal alprostidil
- **D)** Treat with intraurethral alprostidil
- **E)** Treat with PDE-5 inhibitors

Answer

Correct answer : Treat with PDE-5 inhibitors

This man has the features of Peyronie's disease, a condition where fibrous plaques develop within the tunica albuginea of the penis. The consequence is penile tethering producing curvature of the penis during an erection. The condition can be acute or chronic and can contribute to erectile dysfunction. It is relatively common occurring in roughly 3% of males over 50 years (1). Treatment depends on the severity of the disorder and can range from simple observation to corrective surgery. In our case, the man has erectile dysfunction with some curvature which is not painful and is not reported to impede intercourse. The most appropriate initial approach would be treating the erectile dysfunction with conventional PDE-5 inhibitors. (1)

Medscape – Peyronie's disease treatment and management

Question 31

A 50-year-old male is being treated for erectile dysfunction associated with Peyronie's disease of the penis. He has mild penile curvature which does not inhibit intercourse. However, over the last 2 years he has had problems with deteriorating erectile dysfunction. He commenced PDE-5 inhibitors approximately 1 year ago with reasonable effect but has since found that his response to therapy has been disappointing. He has been using maximal doses of vardenafil but has noticed that his erections are still poor and he has been unable to have intercourse over the last 3 – 5 months. Otherwise he is well and takes no other medication. Originally, he was also shown a vacuum device but found that this was uncomfortable and resulted in unfulfilling intercourse.

Which of the following would be the most appropriate approach to treating his erectile dysfunction?

- **A)** Add tadalafil to vardenafil
- **B)** Refer for penile corrective surgery
- **C)** Refer for penile prosthesis
- **D)** Use intracavernosal alprostidil
- **E)** Use intraurethral alprostidil

Answer

Correct answer : Use intraurethral alprostidil

This man has Peyronie's disease and associated erectile dysfunction. Sometimes, there may be an initial satisfactory response to PDE-5 inhibitors, and then this response can decline. Assuming that there is no progression of the Peyronie's disease, as the patient has slight curvature, denies pain and has been able to have intercourse, then the most appropriate second line agent would be intraurethral alprostidil. Typically higher doses are required to achieve a satisfactory erection and occasionally, combined treatment of intraurethral alprostidil and oral PDE-5 inhibitors can provide added benefit (1). Intracevernosal alprostidil should not be used in patients with Peyronie's disease as intracavernosal injections may exacerbate penile fibrosis (2). There is no evidence that combinations of PDE-5 inhibitors are more effective than single drug.

BSSM Guidelines

Question 32

A 19-year-old male presents to clinic concerned about developmental delay. He is worried about poor development of facial and body hair plus poor development of external genitalia. He is well and academically is going to university to study maths. He is rather distressed about his poor development.

On examination, he has a BMI of 22 and is on the 50th centile for height and weight. He has some slight wisps of pubic hair but a small penis of 5cm stretched length and testicular volumes of 5 mls bilaterally. He has no facial hair. He has a normal sense of smell.

Investigations reveal: TFTs, short synacthen and IGF-1 all normal.

		Normal Ranges
Testosterone	<0.7>	(9-30)
LH	1 mu/l	(1-10)
FSH	1 mu/l	(1-10)
Prolactin	300 mu/l	(< />
MRI	Normal	
Karyotype	Normal	

Which of the following is the most appropriate approach to the management of the patient?

- **A)** Observe – no treatment required currently
- **B)** Treat with clomiphene
- **C)** Treat with HCG
- **D)** Treat with IM testosterone
- **E)** Undertake a GnRH stimulation test

Answer

Correct answer : Treat with IM testosterone

This young man has delayed puberty which is causing him distress. The average age of onset of puberty in boys is 12 and in girls is 11. Delayed puberty is defined as no signs of pubertal development in a boy at age 14 and a girl age 13. Usually the first signs of pubertal development are gonadal enlargement in boys and breast buds in girls.

There appears to be no clear cause for this as the patient is eupituitary and MRI is normal. This is therefore isolated GnRh deficiency. The most appropriate approach to the management of this man would be a low dose of of IM testosterone (50mg per month) which may accelerate pubertal development. When testicular size begins to enlarge treatment can be stopped.

Diagnosis and treatment of delayed puberty Authors: William F Crowley, Jr, MD Nelly Pitteloud, MD

Question 33

A 38-year-old woman was referred by her GP with an 11-month history of secondary amenorrhea. She also had hot flushes, mood swings and night sweats. She denied excessive hair growth. She had normal puberty and always had regular periods. She had a past medical history of Hashimoto's thyroiditis and pernicious anaemia for which she had been taking thyroxine and B12 injections. She is a mother of two children and smokes 20 cigarettes per day. On examination, she had a BMI of 26 kg/m^2 with no evidence of hirsutism. Her general and systemic examination was unremarkable.
Further investigations

	Result	Normal Range
FSH	60 mIU/ml	4.7-21.5 mIU/ml
LH	38 IU/L	1.9-12.5 IU/l
Testosterone level	1.4 nmol/L	<2 nmol/l
17 hydroxyprogesterone level	6 nmol/l	3-6 nmol/l
Estradiol	68 pmol/l	130-880 pmol/l

What is the most likely diagnosis?

- **A)** Congenital adrenal hyperplasia
- **B)** Menopause
- **C)** Non-functioning pituitary macroadenoma
- **D)** Polycystic ovarian syndrome
- **E)** Premature ovarian failure

Answer

Correct answer : Premature ovarian failure

Explanation:

Premature ovarian failure (POI) is characterised by amenorrhea, oestrogen deficiency and elevated gonadotrophins as result of a loss of ovarian follicular function before the age of 40.

The majority of the cases are idiopathic (80%.)

Some of the causes include:

Chromosomal abnormalities (5–10%): Turner's syndrome, Fragile X premutations etc

Autoimmune disease (20%)

Iatrogenic: chemotherapy, radiotherapy and pelvic surgery.

Reference:

- Nelson, L.M., 2009. Primary ovarian insufficiency. New England Journal of Medicine, 360(6), pp.606-614

Question 34

A 38-year-old woman was referred by her GP with an 11-month history of secondary amenorrhea. She also had hot flushes, mood swings and night sweats. She denied excessive hair growth. She had normal puberty and always had regular periods. She had a past medical history of Hashimoto's thyroiditis and pernicious anaemia for which she had been taking thyroxine and B12 injections. She is a mother of two children and smokes 20 cigarettes per day.

On examination, she had a BMI of 26 kg/m^2 with no evidence of hirsutism. Her general and systemic examination was unremarkable. Further investigation revealed low estradiol with a very high-level of gonadotrophins.

	Result	Normal Range
FSH	60 mIU/ml	4.7-21.5 mIU/ml
LH	38 IU/l	1.9-12.5 IU/l
Testosterone level	1.4 nmol/l	<2 nmol/l
17 hydroxyprogesterone level	80 ng/dl	100-500 ng/dl
Estradiol	68 pg/ml	130-880 pg/ml

The results were consistent with premature ovarian insufficiency (POI).
The criteria age, below which one establishes a diagnosis of POI is?

- **A)** 30 years
- **B)** 35 years
- **C)** 38 years
- **D)** 40 years
- **E)** 45 years

Answer

Correct answer : 40 years

Explanation:

POI is characterised by amenorrhea, estrogen deficiency and elevated gonadotrophins as a result of loss of ovarian follicular function before the age of 40. The majority of the cases are idiopathic (80%). Some of the causes include:

Chromosomal abnormalities (5–10%): Turner’s syndrome, Fragile X premutations etc

Autoimmune disease (20%)

Iatrogenic: chemotherapy, radiotherapy and pelvic surgery.

Reference:

- Nelson, L.M., 2009. Primary ovarian insufficiency. New England Journal of Medicine, 360(6), pp.606-614

Question 35

A 27-year-old woman presents with a prolonged menstrual cycle that she has been experiencing for the past 6 months, associated with hot flushes and night sweats. Following a serum follicle stimulating hormone (FSH) measurement of 58 U/L and a serum anti-mullerian hormone (AMH) of 0.2 ng/ml, she was diagnosed with premature ovarian failure (POF).
Which is the most likely autoimmune disease associated with POF?

- **A)** Addison’s disease
- **B)** Celiac disease
- **C)** Grave’s disease
- **D)** Rheumatoid arthritis
- **E)** Systemic Lupus Erythematosus (SLE)

Answer

Correct answer : Addison’s disease

Explanation:

POI of adrenal autoimmune origin is the most frequent type observed in 60 to 80% of patients with autoimmune POI. POF is also associated with other autoimmune diseases such as thyroid diseases, hypoparathyroidism, hypophysitis, type 1 diabetes mellitus, and non-endocrine autoimmune diseases, including systemic lupus erythematosus (SLE), Sjogren's syndrome, rheumatoid arthritis, immune thrombocytopenic purpura, autoimmune haemolytic anaemia, pernicious anaemia, etc.

References:

- Silva, C.A., Yamakami, L.Y.S., Aikawa, N.E., Araujo, D.B., Carvalho, J.F. and Bonfá, E., (2014). Autoimmune primary ovarian insufficiency. Autoimmunity reviews, 13(4-5), pp.427-430.
- La Marca, A., Brozzetti, A., Sighinolfi, G., Marzotti, S., Volpe, A. and Falorni, A., (2010). Primary ovarian insufficiency: autoimmune causes. Current Opinion in Obstetrics and Gynecology, 22(4), pp.277-282.

Question 36

A 28-year-old woman is diagnosed with anovulation due to polycystic ovarian syndrome. She does not resume ovulation despite weight loss and metformin use. She goes on to receive three cycles of clomiphene citrate in order to induce ovulation and achieve conception, but suffered ovarian hyperstimulation syndrome and the treatment has now been stopped.
Which of the following is the most appropriate regimen/intervention for ovulation induction in this patient?

- **A)** Aromatase inhibitor (letrozole)
- **B)** Exogenous gonadotropins (purified FSH) at high doses
- **C)** Exogenous gonadotropins (purified FSH) as sequential treatment to clomiphene administration
- **D)** Insulin sensitising agent (thiazolidinediones)
- **E)** Laparoscopic ovarian drilling

Answer

Correct answer : Aromatase inhibitor (letrozole)

Explanation:

Resumption of ovulation in PCOS patients starts with lifestyle changes and metformin use. In cases that these drugs fail to resume ovulation, the next reasonable choice is clomiphene citrate with a dose increase by 50 mg in each subsequent cycle. In case of ovarian hyperstimulation syndrome, treatment should be stopped, and seek other options. Laparoscopic ovarian drilling is not considered as treatment of choice for PCOS anovulation as it has several complications such as adhesion formation and depletion of ovarian reserve. Exogenous gonadotropin preparations are not suitable for women that suffer from OHS as they have increased rates for OHS. If exogenous gonadotropins are used, a low dose step-up approach is advised and not a high doe step down approach. Aromatase inhibitors such as letrozole are a second-line option following clomiphene resistant cases and have comparable pregnancy rates as clomiphene.

References:

- Fisher SA, Reid RL, Van Vugt DA, Casper RF. A randomized double-blind comparison of the effects of clomiphene citrate and the aromatase inhibitor letrozole on ovulatory function in normal women. Fertil Steril 2002;78:280
- Filicori M, Cognigni GE, Pocognoli P, Tabarelli C, Ferlini F, Perri T, Parmegiani L. Comparison of controlled ovarian stimulation with human menopausal gonadotropin or recombinant follicle-stimulating hormone. Fertil Steril 2003;80:390

Question 37

A 25-year-old woman presents with symptoms of hirsutism, acne and oligomenorrhea. Following the diagnosis of polycystic ovarian syndrome she had a series of laboratory examinations to assess biochemical hyperandrogenism, as well as gonadotropin levels. Which of the following best describes the relationship between LH and FSH in PCOS women?

- **A)** LH/FSH <2
- **B)** LH/FSH >2-3
- **C)** FSH/LH > 1.5
- **D)** FSH/LH >4
- **E)** FSH/LH is equal to 1

Answer

Correct answer : LH/FSH >2-3

Explanation:

Biochemical signs of hyperandrogenism is one of the ESHRE criteria for the definition of PCOS. Elevation of testosterone (>100 ng/dl) and decreased SHBG are the two features of this, while FSH remains normal or low while LH is elevated. In many cases, the LH/FSH ratio is increased but it is not part of the criteria as it is not found in all women with PCOS. Approximately 60% of women will have an increase of the LH/FSH ratio, while the remaining 40% will not, and the rate is usually increased by 2-3 times.

References:

- Fauser, B.C.J.M., Tarlatzis, B.C., Rebar, R.W., Legro, R., Balen, A.H., Lobo, R., Carmina, H., Chang, R.J., Yildiz, B.O., Laven, J.S.E. and Boivin, J., 2012. Consensus on women's health aspects of polycystic ovary syndrome (PCOS). Human Reproduction, 27(1), pp.14-24.
- Legro RS, Arslanian SA, Ehrmann DA, et al. Diagnosis and Treatment of Polycystic Ovary Syndrome: An Endocrine Society Clinical Practice Guideline. JClin Endocrinol Metab. 2013 Dec; 98(12): 4565–4592

Question 38

A 25-year-old lady presents with oligomenorrhea and obesity. She was diagnosed with polycystic ovarian syndrome and despite lifestyle changes (diet, exercise) and metformin use, her cycle duration remained 45-60 days.
What are the possible pathophysiological mechanisms involved in PCOS?

- **A)** Hypergonadotropic hypogonadism
- **B)** Hypogonadotropic hypogonadism
- **C)** Hyperinsulinemia
- **D)** Hyperinsulinemia and/or hyperandrogenism
- **E)** Hyperandrogenism and hypoestrogenism

Answer

Correct answer : Hyperinsulinemia and/or hyperandrogenism

Explanation:

PCOS is characterised by hyperandrogenism (elevation of testosterone and decreased SHBG) as well as hyperinsulinemia (insulin resistance). The pathophysiological mechanisms involved are i. Elevation of LH with a normal or low FSH due to GnRH pulsatile secretion pattern, leads to anovulation and hyperandrogenism as follicles reach the antral stage and remain at that as there is no dominant follicle selection and subsequent ovulation. Hyperinsulinemia is present due to an insulin receptor mutation and subsequent tissue insulin resistance. Central obesity that is frequent in these women, is responsible for hyperestrogenism due to peripheral conversion of androgens to estrogens.

References:

- Wilcox, A.J., Dunson, D. and Baird, D.D., (2000). The timing of the "fertile window" in the menstrual cycle: day specific estimates from a prospective study. Bmj, 321(7271), pp.1259-1262.
- Corson, S.L., (1986). Self-prediction of ovulation using a urinary luteinizing hormone test. The Journal of reproductive medicine, 31(8 Suppl), pp.760-763.

Question 39

A 30-year-old man is an amateur bodybuilder. He has a history of androgen (anabolic steroid) abuse for bodybuilding over the last four to five years. He has been in a stable relationship with his girlfriend for three years and they plan to get married soon. He is concerned about the prospects of fathering a child since he has heard that use of anabolic steroids can reduce the chances of fertility.

On clinical examination he has a muscular physique and is well androgenized. His testicular volume is 14 ml bilaterally. He has stopped taking androgens for the last three months. He says he has experienced some change in body composition however he has no other symptoms. His last semen analysis, performed four months ago when he was taking androgens showed azoospermia. What is the best advice you can give him with regards to his chances of fertility?

- **A)** He has no chances of fertility. Androgen abuse leads to permanent damage to seminiferous tubules
- **B)** He is less likely to father a child and the use of human chorionic gonadotropin (HCG) should be considered
- **C)** He is less likely to father a child and the use of human menopausal gonadotropin (HMG) should be considered
- **D)** He is less likely to father a child and the use of recombinant FSH should be considered
- **E)** Stopping the androgen can lead to return of fertility and resumption of sperm production in most young men and no treatment should be required

Answer

Correct answer : Stopping the androgen can lead to return of fertility and resumption of sperm production in most young men and no treatment should be required

Explanation:

The abuse of androgens (anabolic steroids) leads to negative feedback on the hypothalamus and pituitary leading to the suppression of LH and FSH production. This leads to reduced endogenous testosterone production and spermatogenesis. (El Osta et al., 2016) A recent study has shown that stopping the use of anabolic steroids in young men can lead to return of spermatogenesis and endogenous androgen production. Normalization of sperm output can take a mean period of 14 months from the time of stopping the exogenous androgen use. (Shankara-Narayana et al., 2020)

The use of HCG, HMG and Recombinant FSH can improve fertility outcome in such patients, however no study so far has shown that the use of these agents is more useful than the natural return in fertility which can be expected on stopping androgen. Use of these agents may be reserved for those men who continue to have azoospermia or poor sperm quality after withdrawal of anabolic steroids (Shankara-Narayana et al., 2020).

Reference:

- El Osta, R. et al. (2016) 'Anabolic steroids abuse and male infertility', Basic and clinical andrology. BioMed Central, 26, p. 2. doi: 10.1186/s12610-016-0029-4.
- Shankara-Narayana, N. et al. (2020) 'Rate and Extent of Recovery from Reproductive and Cardiac Dysfunction Due to Androgen Abuse in Men', The Journal of Clinical Endocrinology Metabolism. Oxford University Press US, 105(6), p. dgz324.

Question 40

A 34-year-old woman complains of amenorrhoea and hot flushes over the past 6 months, which is attributed to premature ovarian failure. She wants to know her spontaneous chances of conception.

What is the best test to predict the outcome of IVF in this woman?

- **A)** Anti-mullerian hormone (AMH)
- **B)** Estradiol
- **C)** FSH
- **D)** Inhibin
- **E)** LH

Answer

Correct answer : Anti-mullerian hormone (AMH)

Explanation:

AMH is dependent on the ovarian reserve and is a very good indicator of the success of IVF procedures. FSH and oestradiol are also predictive of IVF outcome but AMH is much more sensitive. Inhibin and LH do not have a clinical use for this issue.

References:

- Weenen, C., Laven, J.S., von Bergh, A.R., Cranfield, M., Groome, N.P., Visser, J.A., Kramer, P., Fauser, B.C. and Themmen, A.P., (2004). Anti-Müllerian hormone expression pattern in the human ovary: potential implications for initial and cyclic follicle recruitment. MHR: Basic science of reproductive medicine, 10(2), pp.77-83.
- Faddy, M.J., Gosden, R.G., Gougeon, A., Richardson, S.J. and Nelson, J.F., (1992). Accelerated disappearance of ovarian follicles in mid-life: implications for forecasting menopause. Human reproduction, 7(10), pp.1342-1346.

Question 41

A 26-year-old woman presents with oligomenorrhea and hirsutism for the past 3 years and had been diagnosed with polycystic ovarian syndrome. She was recently diagnosed with primary infertility, related to her condition. She is prescribed metformin and advice on lifestyle changes in order to normalise her cycle.

Which is the most likely mechanism involved that decreases androgen levels following metformin administration in Polycystic ovary syndrome (PCOS)?

- **A)** Decreased IGFBP-1levels
- **B)** Decreased LH levels
- **C)** Decreased SHBG levels
- **D)** Increased oestradiol levels
- **E)** Increased free testosterone levels

Answer

Correct answer : Decreased LH levels

Explanation:

Metformin improves insulin sensitivity by decreasing gluconeogenesis thus decreasing hepatic glucose production, and increasing tissue sensitivity to insulin. It, therefore, reduces hyperinsulinemia, LH levels, free testosterone levels, PAI-1 and endothelin-1 levels in obese women with PCOS.

References:

- Velazquez EM, Mendoza S, Hamer T, Sosa F, Glueck CJ. Metformin therapy in polycystic ovary syndrome reduces hyperinsulinemia, insulin resistance, hyperandrogenemia and systolic blood pressure, while facilitating normal menses and pregnancy. Metabolism 1994;43:647
- Velazquez E, Acosta A, Mendoza SG. Menstrual cyclicity after metformin therapy in polycystic ovary syndrome. Obstet Gynecol 1997;90: 392

Question 42

A 28-year-old woman presents after being unable to conceive for the past 12 months, seeking advice regarding the aetiology of this problem. Her partner had a semen analysis with normal parameters as he previously visited a urologist for the same issue. What is the next step in investigating the cause of infertility in this patient?

- **A)** Antral follicle count and karyotype
- **B)** Diagnostic laparoscopy and hysteroscopy
- **C)** Ovarian reserve assessment
- **D)** Ovulation and tubal patency assessment
- **E)** Transvaginal ultrasound and hysterosalpingography

Answer

Correct answer : Ovulation and tubal patency assessment

Explanation:

Inability to conceive after a period of 12 months of unprotected intercourse is defined as infertility. This requires investigation of possible female and male factor infertility. Ovulation and tubal patency investigations (ovulation tests, HSG and/or laparoscopy) are the basic female infertility investigations needed while a semen analysis is the basic male infertility investigation required. Ovulation assessment includes menstrual history, basal body temperature, antral follicle count and dominant follicle sonographic assessment, serum FSH and AMH, as well as LH surge assessment. Tubal patency assessment is performed by hysterosalpingography (HSG) as a first step, while laparoscopy is required in suspected tubal blockage and as part of the advanced investigation of an infertile woman. Antral follicle count is part of the ovarian reserve assessment, while a transvaginal ultrasound is not the modality of choice to investigate tubal patency.

References:

- Isaksson, R. and Tiitinen, A., (2004). Present concept of unexplained infertility. Gynecological endocrinology, 18(5), pp.278-290.
- Gelbaya, T.A., Potdar, N., Jeve, Y.B. and Nardo, L.G., (2014). Definition and epidemiology of unexplained infertility. Obstetrical & gynecological survey, 69(2), pp.109-115.

Question 43

A 49-year-old woman presents after experiencing amenorrhoea, hot flushes and vaginal dryness for the past 12 months. She seeks treatment for her symptoms as they are affecting her everyday life. You explain to her that hormone replacement therapy (HRT) can lead to severe side effects and she should therefore be investigated prior to administration.
What is the most important clinical assessment required prior to administration of HRT?

- **A)** Bone density assessment
- **B)** Cardiovascular disease and breast cancer risk assessment
- **C)** Endometrial cancer risk assessment
- **D)** Liver and kidney function assessment
- **E)** Venous thromboembolism risk assessment

Answer

Correct answer : Cardiovascular disease and breast cancer risk assessment

Explanation:

HRT administration requires CVD and breast cancer risk assessment prior to administration due to their possible side effects. All other options require investigation prior to administration if any signs and symptoms are present (unexplained vaginal bleeding, elevation of liver enzymes, history of DVT/PE, etc).

References:

- Lisabeth, L.D., Beiser, A.S., Brown, D.L., Murabito, J.M., Kelly-Hayes, M. and Wolf, P.A., (2009). Age at natural menopause and risk of ischemic stroke: the Framingham heart study. Stroke, 40(4), pp.1044-1049.
- American College of Obstetricians and Gynecologists, (2014). Management of menopausal symptoms. Practice Bulletin No. 141. Obstet Gynecol, 123, p.202.

Question 44

A 21-year old woman presents with secondary amenorrhoea for the past 6 months. She mentions that this started at a time of great stress due to loss of employment. A pregnancy test is negative and a hormonal profile examination is requested to confirm if this is the cause of amenorrhoea.

Which is the most probable endocrine abnormality related to stress amenorrhoea?

- **A)** Decreased cortisol
- **B)** Decreased ACTH
- **C)** increased CRH
- **D)** Increased GnRH
- **E)** Increased TRH

Answer

Correct answer : increased CRH

Explanation:

Stress amenorrhoea is associated with elevation of CRH probably due to decreased leptin and increased neuropeptide Y due to concurrent weight loss, which is unable to suppress the stress-induced CRH secretion. CRH in turn increases cortisol, which further increases weight loss. Endorphins, ACTH and cortisol are also increased, while TRH, TSH and T4 are decreased.

References:

- Bullen BA, Skriinar GS, Beitins IZ, et al. Induction of menstrual disorders by strenuous exercise in untrained women. New Engl J Med 1985;312:1349
- Tofler IR, Stryek BK, et al. Physical and emotional problems of elite female gymnasts. New Engl J Med 1996;335:281

Question 45

A 35-year-old man was referred by his GP to an endocrine clinic after he was diagnosed with Kallmann's syndrome. The patient was concerned about the risk of transmission of disease to his offspring.

Which genetic mutation is associated with a 50% risk of transmission to his offspring?

- **A)** FGFR1
- **B)** KAL1
- **C)** KAL4
- **D)** NELF
- **E)** PROK2

Answer

Correct answer : FGFR1

Explanation:

Kallmann's syndrome is a genetic disorder characterised by failure of episodic GnRH secretion due to disordered migration of GnRH producing neurons into hypothalamus resulting in secondary hypogonadism (low testosterone, LH and FSH levels). Anosmia is present in 75%. There is an increased risk of cleft lip and palate, sensorineural deafness, cerebellar ataxia and renal agenesis. It may be inherited in a X-linked recessive (KAL1 gene mutation), autosomal dominant (FGFR1/ KAL2 gene mutation) or autosomal recessive trait (PROK2 gene mutation). There is a 50% risk of transmission to offspring in males with FGFR1 mutation while KAL1 is linked with a more severe reproductive phenotype.

Reference:

- Wass, J. and Owen, K. (2014) Oxford handbook of Endocrinology and Diabetes. 3rd edn. Pakistan: Oxford University Press.

Question 46

A 17-year-old female was referred to the endocrinologist for primary amenorrhoea. On examination, she was 148 cm tall and had a webbed neck with poor development of secondary sexual characteristics. Her hormonal profile revealed the following:

Estradiol	45 pmol/L	(69-905)
FSH	48 U/L	(2.5-10.2)
LH	40U/L	(1.9-12.5)

She was referred for karyotyping, which revealed 45,X/46,XY. Considering the diagnosis, what risk is associated with the given karyotype?

- **A)** Cardiac abnormalities
- **B)** Gonadoblastoma
- **C)** IBD
- **D)** Sensorineural hearing loss
- **E)** Thyroiditis

Answer

Correct answer : Gonadoblastoma

Explanation:

This patient has short stature, webbed neck and primary amenorrhoea due to gonadal failure (low oestrogen and raised FSH and LH). These features are suggestive of Turner’s syndrome. Turner's syndrome is the most common X chromosome abnormality in females and has various karyotypes. Each karyotype has particular phenotypic characteristics and risks. 45,X/46,XY is associated with an increased risk of gonadoblastoma needing gonadectomy, while thyroiditis, IBD and sensorineural hearing loss are associated with 46,Xi(Xq). There is a high incidence of renal and cardiac abnormalities with karyotype 45,X.

Reference:

- Wass, J. and Owen, K. (2014) Oxford handbook of Endocrinology and Diabetes. 3rd edn. Pakistan: Oxford University Press

Question 47

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- **D)** Sensorineural hearing loss
- **E)** Thyroiditis

Answer

Correct answer : Gonadoblastoma

Explanation:

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Reference:

- Wass, J. and Owen, K. (2014) Oxford handbook of Endocrinology and Diabetes. 3rd edn. Pakistan: Oxford University Press

Question 1

A 47 year old female is referred by her GP as she has a 3 month history of headaches and tiredness. She has a 5 year history of bipolar disorder for which she takes lithium and olanzapine. She has regular menses and no galactorrhoea. On examination, there is nil to find. The GP includes the following biochemistry:

LH	2.2 mu/l (2-10)
FSH	3.1 mu/l (2-10)
Estradiol	280 pmol/l (150-800)
Prolactin	1450 mu/l (<500)

What is the likely cause of her hyperprolactinaemia?

- **A)** Drug-induced
- **B)** Microprolactinoma
- **C)** Macroprolactinoma
- **D)** Polycystic ovarian syndrome
- **E)** Stress

Answer

Correct answer : Drug-induced

This patient is taking a dopamine antagonist – olanzapine which will cause hyperprolactinaemia. The fact that the menstrual function is normal and estradiol is normal would argue against the hyperprolactinaemia being pathological due for instance, to a microprolactinoma.

Reference:

Drug-induced hyperprolactinaemia

Question 2

A 72 year old female is diagnosed with acromegaly due to a macroadenoma of the pituitary and underwent surgery. Surgical resection was unsuccessful, no further surgery was recommended and she had received radiotherapy 2 years ago. However, her growth hormone concentrations on day profile and IGF-1 concentrations remain elevated despite the use of octreotide LAR 30 mg every 4 weeks.

Which of the following is the most appropriate management for this patient's ongoing acromegaly?

- **A)** Dopamine agonist therapy
- **B)** Further radiotherapy
- **C)** Increase dose of octreotide
- **D)** Pegvisomant
- **E)** Switch to lanreotide

Answer

Correct answer : Pegvisomant

This patient has active acromegaly which is refractory to somatostatin analogue therapy. In this case the most appropriate treatment could be pegvisomant, a GH receptor blocker which therefore reduces the production of IGF-1, the hormone through which most of the actions of GH are mediated.

Question 3

A 23 year old female presents with a two year history of failure to conceive and oligomenorrhoea. She is investigated, found to have a prolactin of 1015 mu/l (50-500) and is diagnosed with a microprolactinoma. She explains that she is keen to conceive.
Which of the following is the most appropriate treatment for this patient?

- **A)** Bromocriptine
- **B)** Cabergoline
- **C)** Pituitary surgery
- **D)** Radiotherapy
- **E)** Somatostatin analogues

Answer

Correct answer : Bromocriptine

Bromocriptine is the treatment for hyperprolactinaemia that is licensed for use in patients wishing to conceive. Quinagolide is also licensed but cabergoline is not licensed despite there being evidence of its safety with conception. However, bromocriptine is the drug that is advocated if the patient informs you of her desire to become pregnant. Surgery is rarely required for the treatment of prolactinomas.

Question 4

A 45 year old female is being treated for a prolactinoma and has been receiving cabergoline at a dose of 4 mg twice weekly. However, the prolactin concentration remains elevated at 15,000 mu/l (although there was an initial decline of prolactin levels from 70,000 mu/l at initial presentation). This has not fallen since the dose was increased to 2 mg twice weekly. She remains amenorrhoeic. Her most recent MRI scan reveals that the tumour has shrunk since the original scan of 3 months ago but she still has a 2 cm pituitary tumour which is just touching the chiasm. Her visual fields are full to confrontation.
Which of the following is the most appropriate treatment for this patient?

- **A)** Add bromocriptine to cabergoline
- **B)** Advise pituitary surgery
- **C)** Advise pituitary radiotherapy
- **D)** Increase dose of cabergoline further
- **E)** Switch cabergoline to bromocriptine

Answer

Correct answer : Advise pituitary surgery

This patient appears to have dopamine agonist-resistant prolactinoma and no further benefit can be gained from further dose increase, as the prolactin concentration hasn't fallen despite gradual dose titration. The most appropriate treatment would be surgery and possibly radiotherapy thereafter depending on the success of surgery.

Question 5

A 72 year old female is receiving treatment with pegvisomant for acromegaly which is unresponsive to somatostatin analogues. What is the mechanism of action of pegvisomant?

- **A)** GH receptor antagonist
- **B)** GHRH receptor antagonist
- **C)** Highly selective dopamine agonist
- **D)** IGF-1 receptor antagonist
- **E)** Somatostatin receptor agonist

Answer

Correct answer : GH receptor antagonist

pegvisomant is a GH receptor blocker and results in a decline in IGF-1 concentrations in active acromegaly. It is generally reserved for the treatment of active acromegaly that is resistant to somatostatin analogues.

Question 6

A 40 year old female undergoes MRI by the ENT surgeons as an investigation of episodic balance problems. No abnormality is noted of the posterior fossa or auditory apparatus but incidental note is made of a 5 mm microadenoma of the pituitary. The patient has no symptoms nor are there any signs of endocrine disorder.
Investigations reveal:

		Normal Ranges
Estradiol	550 pmol/l	(130 - 800)
LH	2.2 mu/l	(2 - 10)
FSH	3.3 mu/l	(2 - 100)
Prolactin	410 mu/l	(<450)
24hr urine free Cortisol	188 nmol/d	(<280)
TSH	2.2 mu/l	(0.5 - 4.5)
IGF-1	28.9 nmol/l	(22 - 40)

Which of the following is the most appropriate management strategy for this patient?

- **A)** Arrange insulin tolerance test
- **B)** Arrange oral glucose tolerance test
- **C)** Arrange repeat MRI in 1 year
- **D)** Reassure and discharge
- **E)** Refer for pituitary surgery

Answer

Correct answer : Arrange repeat MRI in 1 year

This patient has an incidentally noted pituitary microadenoma and the investigations suggest that this is non-functional. Hypopituitarism is most unlikely based on the size and absence of symptoms and an insulin stress test (IST) is not warranted. The normal IGF-1 concentration is an excellent test for acromegaly and its normality would exclude this diagnosis in an otherwise healthy person.

Studies suggest that microadenomas rarely enlarge (<10%) and so with this in mind, a further MRI should be arranged for 1 year and if there is no evidence of progression, then imaging can be done infrequently. Guidelines

Question 7

A 55 year old male is reviewed after referral from the general physicians. He was investigated for a vague headache and had a CT scan which quite co-incidentally revealed a pituitary macroadenoma. An MRI subsequently reports a 2 cm macroadenoma which encroaches upon the optic chiasm. There are no obvious abnormalities to suggest endocrine dysfunction on examination and his visual field assessment is entirely normal. His investigations reveal:

		Normal Ranges
Cortisol response to short synacthen test	840 nmol/l	(>550)
Thyroid function test	Normal	
Prolactin	780 mu/l	(<450)
LH	3.3 mu/l	(2 - 10)
FSH	2.8 mu/l	(2 - 10)
Testosterone	7.8 nmol/l	(8 - 30)
IGF-1	12.9 nmol/l	(18 - 33)

What is the most appropriate management for this patient?

- **A)** Refer for pituitary radiotherapy
- **B)** Refer for pituitary surgery
- **C)** Repeat MRI in 6 months
- **D)** Treat with bromocriptine
- **E)** Treat with cabergoline

Answer

Correct answer : Refer for pituitary surgery

This patient has a co-incidentally noted pituitary adenoma which does impinge on the optic chiasm. Despite the normal visual fields the most appropriate treatment would be surgical removal, as, considering his young age, it is likely to grow and pose a threat to his vision. The slightly elevated prolactin does not mean that the patient has a prolactinoma - this is likely to reflect stalk compression and dopamine agonist therapy would be ineffective.

Question 8

A 28 year old female who is 30 weeks pregnant presents with profound tiredness and lethargy. She is noted to have a sodium of 130 mmol/l on routine testing and this sparks further investigation.

Her investigations reveal:

An MRI of the pituitary is performed which reveals enlargement of the pituitary bulging slightly beyond the sellar but with no obvious tumour.

Which of the following is the likely diagnosis?

		Normal Ranges
Cortisol post short synacthen test	252 nmol/l	(>550)
Free thyroxine	5.5 pmol/l	(9-22)
TSH	2.2 mu/l	(0.5 - 5)
Prolactin	3300 m/l	(<450)
estradiol	1300 pmol/l	(130 - 800)
LH	1.1 mu/l	(2 - 10)
FSH	1.0 mu/l	(2 - 10)

- **A)** Dysgerminoma
- **B)** Lymphocytic hypophysitis
- **C)** Non-functioning pituitary tumour
- **D)** Prolactinoma
- **E)** Silent pituitary infarction

Answer

Correct answer : Lymphocytic hypophysitis

This pregnant woman presents in the third trimester with a hyponatraemia, secondary hypothyroidism, an appropriate prolactin and oestradiol concentrations for this stage of pregnancy and an inadequate cortisol response to synacthen. This suggests partial hypopituitarism during the latter stages of pregnancy which is likely due to lymphocytic hypophysitis. Even without the MRI, pituitary tumour is unlikely as the patient became pregnant - unlikely if there was pre-existent hypopituitarism associated with a pituitary tumour either functional or non-functional.

Question 9

A 19 year old male with childhood onset idiopathic hypopituitarism was referred to the adult endocrine clinic. He had received growth hormone and testosterone gel for the last 6 years and had grown to an appropriate adult height and had normal secondary sexual characteristics. Investigations reveal:

		Normal Ranges
IGF-1	42.3 nmol/l	(28 - 50)
Testosterone	15.5 nmol/l	(9 - 30)
LH	1.2 mu/l	(2 - 10)
FSH	2.2 mu/l	(2 - 10)
Free T4	14.5 pmol/l	(9 - 22)
TSH	2.2 mu/l	(0.5 - 5)
Prolactin	360 mu/l	(50 - 450)

He is keen to continue GH therapy but is aware that if this is no longer necessary he is prepared to stop it. Which of the following is the most appropriate action for this patient concerning his GH therapy?

- **A)** Continue GH at its current dose
- **B)** Increase dose of GH
- **C)** Re-assess GH secretion
- **D)** Reduce dose of GH
- **E)** Stop GH therapy

Answer

Correct answer : Re-assess GH secretion

Approximately 30% of subjects shown to be GH deficient in childhood subsequently have normal GH secretion in adulthood. Thus, it is recommended that all subjects should be re-tested for GH deficiency in adulthood. If intact, the GH can be discontinued. If however GH deficiency persists then GH should continue, particularly if the patient subjectively feels improvement (assessed through AGHDA questionnaire) and also as it contributes to the attainment of peak bone mass.

Question 10

A 22 year old male is referred to the endocrine clinic by the GP. He has a history of craniopharyngioma for which he takes full hormone replacement therapy including thyroxine 150 mg daily, hydrocortisone 10 mg bd and testosterone gel 60 mg daily. He is well, but his GP refers him to you as he is concerned by the attached thyroid function tests:

		Normal Ranges
Free T4	15.5 pmol/l	(9 - 22)
TSH	<0.02	(0.5 - 4.5)

There are no abnormalities to find on clinical examination of this patient.
Which of the following is the most appropriate action for this patient?

- **A)** Leave dose of thyroxine unchanged
- **B)** Reduce dose of thyroxine to 100 micrograms/d
- **C)** Reduce dose of thyroxine to 125 micrograms/d
- **D)** Request free T3 concentration
- **E)** Request TSH receptor antibodies

Answer

Correct answer : Leave dose of thyroxine unchanged

This is a frequent GP request. The important thing to recognise is that the patient is hypopituitary and so one cannot rely on TSH measurement. Therefore, the dose of thyroxine should be sufficient to aim for a thyroid hormone concentration in the mid to upper half of the normal range. This patient is stated to be well without any reported features of thyroid hormone excess – there is no need to measure free T3 and the dose of thyroxine should be left unchanged.

Question 11

A 22 year old male is referred by his GP with tiredness. Since the age of 5 he was treated for hypothyroidism and has had poor growth. He is currently receiving 100 micrograms of thyroxine daily. He is of short stature but has normal pubertal development. His investigations reveal:

		Normal Ranges
Free T4	14.6 pmol/l	(9 - 22)
TSH	0.5 mu/l	(0.5 - 5)
Testosterone	12.9 nmol/l	(9 - 30)
LH	2.8 mu/l	(2 - 10)
FSH	3.2 mu/l	(2 - 10)
IGF-1	5.2 nmol/l	(28 - 50)
Prolactin	33 mu/l	(50 - 450)
Cortisol post-synacthen	850 nmol/l	(>550)

CT of the head reports no abnormality of the pituitary.
What is the most appropriate investigation for this patient?

- **A)** Request KAL-1 mutational analysis
- **B)** Request MENIN mutational analysis
- **C)** Request MRI of the pituitary and olfactory bulbs
- **D)** Request Pit-1 mutational analysis
- **E)** Request SOX-1 mutational analysis

Answer

Correct answer : Request Pit-1 mutational analysis

It is rather unusual for a young child to have developed primary hypothyroidism and what is more this adult is now short with a low IGF-1 suggesting GH deficiency and a low prolactin suggesting hypoprolactinaemia. This would suggest a combined partial hypopituitarism - TSH, PRL and GH typical of a mutation of the transcriptional activator - pit-1. Prop-1 mutations (Prophet of Pit-1) are the most common defects in combined childhood pituitary hormone deficiencies and are characterised by LH/FSH deficiency together with GH, TSH and Prolactin. Later, ACTH deficiency may ensue. Imaging may reveal a small or indeed normal appearance of the pituitary and will tell us nothing of the functionality.

Question 12

A 44 year old male is diagnosed with a pituitary macroadenoma. He undergoes trans-sphenoidal resection of this lesion and the histology is reported as a chromophobe adenoma. Which of the following would be the likely cause of this histological description?

- **A)** ACTH secreting adenoma
- **B)** GH secreting tumour
- **C)** Non-functional adenoma
- **D)** Prolactinoma
- **E)** TSH secreting adenoma

Answer

Correct answer : Non-functional adenoma

A chromophobe adenoma does not take up any dye – chromophobe. Hence this is typical of a non-functional pituitary tumour. Eosinophilic adenomas are typically GH or prolactin producing whereas basophilic describe ACTH tumours.

Question 13

A 33 year old female with a diagnosis of acromegaly due to a microadenoma has been treated with monthly depot somatostatin analogues. Her GH day profile concentrations and IGF-1 are as follows:

		Normal Ranges
GH day profile all results		<2 mu/l
IGF-1	22.8 nmol/l	(15-40)

She now presents to clinic and explains that she is 8 weeks pregnant. What do you advise regarding her management?

- **A)** Advise surgery
- **B)** Continue somatostatin analogue therapy at current dose
- **C)** Increase dose of somatostatin analogue therapy
- **D)** Stop depot somatostatin analogue therapy
- **E)** Switch to tds short acting analogue somatostatin therapy.

Answer

Correct answer : Stop depot somatostatin analogue therapy

SMS analogue therapy is not licensed for pregnancy and should be stopped. In this scenario, with the patient being effectively cured with SMS therapy in the presence of a microadenoma, it would seem most appropriate to stop analogue therapy. However, many experts, particularly in the context of a macroadenoma may take the approach of continuing treatment as no ill effects have been reported. This is quite an unusual scenario as surgery would have been considered as a first line treatment for acromegaly, yet many young women who may wish to begin a family, may elect SMS analogues in the first instance as the risks of hypopituitarism after surgery are quite high.

Question 14

A 33 year old female presents one month after giving birth to a baby boy. She has been diagnosed with a microprolactinoma and has been treated with cabergoline 0.25mg twice weekly. Shortly after commencing cabergoline she fell pregnant and the cabergoline was stopped. She had no problems during pregnancy and now is breast feeding. She now enquires as to the most appropriate management strategy relating to the ongoing treatment of her microprolactinoma. Her visual fields are normal to confrontation. Her results reveal:

		Normal Ranges
Prolactin	1040 mu/l	(50-450)
TFTs	Normal	

Which do you advise?

- **A)** Arrange pituitary MRI
- **B)** Commence quinagolide
- **C)** Commence bromocriptine
- **D)** Recommence cabergoline
- **E)** No intervention required

Answer

Correct answer : No intervention required

This patient has been successfully treated with cabergoline and has conceived following treatment. The patient is well and continues to breastfeed. The high prolactin is typical of the postpartum period and in view of the patient’s desire to continue breast feeding and in the absence of any particular problems suggestive of expansion of the prolactinoma, there is no need for any intervention.

Question 15

A 52 year old male is referred as his GP had organised a DEXA scan for him as he had been concerned about his bone thickness. This concern had arisen as he had read about reduced bone mineral density in relation to hypopituitarism. Ten years ago he had surgical removal of a non-functional pituitary macroadenoma and had developed hypopituitarism for which he receives hydrocortisone 10 mg bd, thyroxine 150 micrograms daily and testogel 50 mg daily. His DEXA scan reveals T scores of -2.6 in some areas of the lumbar spine and -2.4 in the hip. He is generally fit and quite well but, after reading an article on bone strength in hypopituitarism is concerned about osteoporosis.
His other investigations reveal:

		Normal Ranges
IGF-1	10.8 nmol/l	(28-42)
Testosterone	14.5 nmol/l	(9-30)
FreeT4	18.2 nmol/l	(9-23)
TSH	0.07 mu/l	(0.5-5)

Which of the following is the most appropriate management of his DEXA result?

- **A)** Growth hormone therapy
- **B)** Increase dose of testogel
- **C)** No specific treatment required
- **D)** Reduce dose of thyroxine
- **E)** Weekly alendronate

Answer

Correct answer : Weekly alendronate

The most appropriate approach to treating this man’s osteoporosis, as demonstrated with a T score of less than -2.5, is a bisphosphonate such as weekly alendronate. The causes of low bone mass density (BMD) in association with hypopituitarism are multi-factorial and growth hormone (GH) deficiency may contribute. Although this man is highly likely to have GH deficiency as demonstrated by his low IGF-1, he does not appear to have specific symptoms of GH deficiency that might merit treatment and NICE do not advocate the use of GH as a treatment of reduced BMD in adults hypopituitary patients. Unlike bisphosphonates, where there is evidence of reduced fracture risk, GH therapy has no data of reduced fracture risk.

Question 16

A patient is suspected of having acromegaly and undergoes an oral glucose tolerance test. The results of this are shown:

Time	0	120 minutes
Glucose (mmol/l)	5.6	8.8
Growth Hormone (mu/l)	4.4	5.5

Which of the following is the correct interpretation of this test?

- **A)** Acromegaly and diabetes mellitus
- **B)** Acromegaly and impaired glucose tolerance
- **C)** Acromegaly and normal glucose tolerance
- **D)** Normal growth hormone (GH) response and impaired glucose tolerance
- **E)** Normal results

Answer

Correct answer : Acromegaly and impaired glucose tolerance

This patient has a paradoxical rise in GH concentrations during the oral glucose tolerance test (OGTT) and this indicates acromegaly as the GH concentrations should suppress below 1mcg/l or 1ng/ml. With regard to the glucose concentrations, the glucose at 120 mins is 8.8 mmol/l indicating impaired glucose tolerance.

Question 17

A 43 year old man underwent a resection of a non-functional pituitary tumour. Post-operatively he had developed seizures which had been treated with sodium valproate. He is also receiving hydrocortisone and thyroxine. Despite treatment he has felt tired and frequently lethargic following the procedure. Which of the following would be the most appropriate test to confirm a suspected diagnosis of growth hormone deficiency?

- **A)** Clonidine test
- **B)** GHRH/Arginine test
- **C)** Glucose tolerance test
- **D)** IGF-1 concentration
- **E)** Insulin tolerance test

Answer

Correct answer : GHRH/Arginine test

The most appropriate test is the GHRH/Arginine test. The patient is being treated with valproate for seizures and so, the insulin tolerance test, a gold standard for the diagnosis of GH deficiency, is contra-indicated. Whilst IGF-1 concentration may support a diagnosis of GHD in panhypopituitary patients, this man dIsn't panhypopituitary as he is not taking testosterone supplementation. Therefore in this case one would undertake dynamic testing and GHRH/ Arginine would be the most appropriate choice vs the glucagon stimulation test which is more cumbersome to undertake and is also less tolerable for the patient.

Question 18

A 44 year old female presents with amenorrhoea, weight gain and ease of bruising. She is diagnosed with Cushing's syndrome based on elevated 24 hr urine free cortisol concentrations of 880 nmol/d (<250) and a cortisol of 88 nmol/l after low dose dexamethasone test. An ACTH is 108 ng/l (20-60). An MRI is performed of the pituitary and is reported as normal. Which of the following is the most appropriate next step for this patient?

- **A)** Domperidone test
- **B)** CT scan of adrenals
- **C)** Inferior petrosal sinus sampling
- **D)** Octreotide scan
- **E)** Pituitary exploration

Answer

Correct answer : Inferior petrosal sinus sampling

These results point to an adrenocorticotropic hormone (ACTH) dependent Cushing's syndrome. It is possible that this could be ectopic although it seems unlikely. Often the MRI does reveal no abnormality but one would want to ensure that one is dealing with pituitary dependent Cushing's syndrome and IPSS would do this. A gradient of above 3:1 central to peripheral ACTH would clinch the diagnosis and sensitivity is improved following CRF.
High dose dexamethasone was once considered to differentiate between Cushing's disease and ectopic but this has proven not to be the case and generally the test adds little to results of Low dose testing and so is used infrequently. CT of adrenals would not provide diagnostic information as it is ACTH dependent disease.

Question 19

A 66 year old male with a past history of ischaemic heart disease and episodes of ventricular tachycardia (VT) has been treated with amiodarone 200 mg for two years. His VT is well controlled on this treatment but latterly he presents with fatigue, anxiety and weight loss.
On examination, he has a fine tremor of the outstretched hands, a pulse rate of 88 bpm but is receiving beta blockers, has lid lag but no goitre is palpable. His thyroid function tests reveal:

		Normal Ranges
Free T4	55 pmol/l	(10-23)
TSH	<0.02	(0.5-5)
Thyroid Antibodies	Negative	

Which of the following is the likely diagnosis?

- **A)** Amiodarone induced thyrotoxicosis type 1
- **B)** Amiodarone induced thyrotoxicosis type 2
- **C)** De Quervain's thyroiditis
- **D)** Graves' disease
- **E)** Hashitoxicosis

Answer

Correct answer : Amiodarone induced thyrotoxicosis type 2

The most likely diagnosis is amiodarone induced thyrotoxicosis type 2 – this is a thyroiditis type picture with thyroid follicle inflammation and release of stored thyroxine. The most appropriate treatment is prednisolone and beta blockade and if possible withdrawal of amiodarone. This contrasts with AIT type 1 where the patient typically has pre-existent thyroid disease or positive thyroid autoantibodies. A thyroid uptake scan may be useful in differentiating between the two as in AIT type 1 uptake may be increased and low in type 2, but this is not often the case as uptake is typically very low due to competition of radio-iodine with the iodine in amiodarone.

Question 20

A 28 year old male with hypopituitarism due to a non-functioning pituitary tumour now wishes to start a family. He underwent surgery at the age of 20 and since has been treated with Testosterone gel 50 mg daily, hydrocortisone 10 mg bd, thyroxine 100 micrograms daily and growth hormone 1.5 mg daily. He has normal erectile function but a most recent semen analysis demonstrates azoospermia.

Which of the following is the most appropriate approach to fertility on this man?

- **A)** Continue testosterone and commence HCG injections
- **B)** Refer for ICSI
- **C)** Refer for sperm donation
- **D)** Stop testosterone and commence clomiphene
- **E)** Stop testosterone and commence HCG injections

Answer

Correct answer : Stop testosterone and commence HCG injections

This patient desires fertility but has hypogonadotropic hypogonadism. The patient should stop testosterone, as this may be associated with impaired spermatogenesis and commence HCG injections. This approach should initially stimulate testosterone production and then sperm production. Often co-prescription of FSH is required. If one fails to stimulate testosterone then it is unlikely that sperm can be generated and referral for ICSI or alternative fertility treatments may be necessary.

Question 21

NICE guidance recommends the use of insulin tolerance test in the investigation of potential growth hormone deficiency (Level 1a). Based upon which of the following does level 1a evidence pertain?

- **A)** Case-control study
- **B)** Non-consecutive studies
- **C)** Systematic review of case control studies
- **D)** Systematic review of randomized control trials
- **E)** Systematic reviews of cohort studies

Answer

Correct answer : Systematic review of randomized control trials

The levels of evidence include 1abc, 2 abc, 3ab, 4 and 5 and are used to grade recommendations. Level 1a is superior and based on systematic reviews of RCTs. 1b is based on one quality RCT.

Question 22

A 55 year old male has been treated for hypopituitarism following surgical resection of a non-functional pituitary tumour 2 years ago. He feels generally tired despite receiving treatment with thyroxine 100 micrograms daily, hydrocortisone 10 mg bd and testosterone gel 50mg daily. His investigations reveal:

		Normal Ranges
Free T4	18.6 pmol/l	(9-23)
TSH	<0.05	(0.5-5)
Prolactin	50 mu/l	(<450)
Testosterone	12.8 nmol/	(9-30)
IGF-1	12.5 nmol/l	(28-42)

Which of the following is the most appropriate treatment for this patient?

- **A)** Commence fludrocortisone
- **B)** Commence growth hormone
- **C)** Increase dose of testosterone
- **D)** Increase hydrocortisone to 30mg daily
- **E)** Reduce dose of thyroxine

Answer

Correct answer : Commence growth hormone

Growth hormone (GH) deficiency is the most likely diagnosis here and is responsible for the tiredness. All other hormones appear to be appropriately replaced – the suppressed TSH is not due to over-replacement of thyroxine but is a consequence of the hypopituitarism. The dose of hydrocortisone is likely typically adequate at 10 mg bd.

GH therapy is associated with improvements in energy as well as wellbeing and should be monitored through IGF-1 maintaining this in the upper half of the age related normal range.

Question 23

A 42 year old hypopituitary male is being treated with thyroxine 100 micrograms daily, hydrocortisone 10 mg bd, testosterone gel and has just commenced growth hormone therapy. Which of the following is the most appropriate for monitoring his response to growth hormone (GH) therapy?

- **A)** AGHDA quality of life score
- **B)** Bioelectrical impedance analysis
- **C)** DEXA scanning
- **D)** PGWBI questionnaire
- **E)** SF-36 form

Answer

Correct answer : AGHDA quality of life score

NICE recommend the monitoring of the effectiveness of GH therapy with the AGHDA score. Patients should begin with an AGHDA score above 11 which reflects a poor quality of life – (normal scores are 4 or less). Treatment should result in an improvement by 7 or more points following adequate treatment for 9 months.

Question 24

A 43 year old male with hypopituitarism due to previous treatment of a non-functional adenoma 5 years ago presents to the clinic complaining of persistent tiredness and lethargy. He also has a history of recently treated hypertension and had a fit postoperatively but continues to be fit free over the last three years whilst taking anticonvulsants. He is receiving hydrocortisone 10 mg bd, thyroxine 100 micrograms daily, testosterone gel 50 mg daily, atorvastatin 10 mg daily, amlodipine 5 mg daily and also sodium valproate 800 mg daily. He is likely to have adult growth hormone (GH) deficiency and would be a candidate for GH therapy. Which of the following would be the most appropriate investigation for the confirmation of GH deficiency in this patient?

- **A)** Clonidine test
- **B)** GHRH/Arginine test
- **C)** Glucagon test
- **D)** IGF-1 concentration
- **E)** Insulin tolerance test

Answer

Correct answer : IGF-1 concentration

In this case the patient already has three hormone deficiencies and is on replacement. If his serum IGF-1 levels are below normal range then associated GH deficiency is confirmed and there will be no need for stimulatory tests. Reference : https://www.aace.com/files/growth-hormone-guidelines.pdf

Question 25

A 45 year old male is being treated for a prolactinoma with cabergoline 1.5mg twice weekly. Original MRI of the pituitary one year ago revealed a 1.3 cm macroprolactinoma which approached but did not compress the optic chiasm. He was commenced on cabergoline and the dose has been gradually increased and he tolerates medication well. On examination, he appears well and his visual fields are entirely full to confrontation. You note that his prolactin has fallen from an original concentration of 30,000 mu/l to its current level of 150 mu/l (50-500).

Which of the following investigations should be undertaken?

- **A)** 24hr ECG
- **B)** CT pituitary
- **C)** Echocardiography
- **D)** MRI pituitary
- **E)** Thrombophilia screen

Answer

Correct answer : Echocardiography

Recent recommendations from the MHRA suggest that all patients being treated with dopamine agonists such as bromocriptine, pergolide and cabergoline should have echo to assess for potential cardiac fibrosis. Although this is disputed by authorities in endocrinology, the recommendations now state that all patients should have an echocardiogram 3-6 months after commencing these ergot-derived dopamine agonists and then at least annually to assess for any evidence of valvular fibrosis and dysfunction. This patient has been successfully treated with cabergoline and shrinkage of the tumour would be expected commensurate with the fall and normalisation of prolactin. There is no need for a MRI.

Reference:

https://www.gov.uk/drug-safety-update/ergot-derived-dopamine-agonists-risk-of-fibrotic-reactions

Question 26

A 32 year old female is 2 weeks postpartum and presents with considerable fatigue and failure to lactate. She is para 2, gravida 2 and her second pregnancy and delivery were relatively uneventful giving birth to a healthy baby boy. During the last trimester she did feel particularly tired and this did differ from her previous pregnancy. She had a normal standard vaginal delivery and did not require any blood post delivery although was told that she was slightly anaemic during her pregnancy. On examination, her blood pressure is 94/66 mmHg and her pulse is 70 bpm with a BMI of 25 kg/m^2. Her investigations reveal:

		Normal Ranges
Free T4	8.1 pmol/l	(9.8 – 23)
TSH	1.5 mu/l	(0.35-5)
Prolactin	<50	(50-450)
Estradiol	<100	(130 – 850)
LH	1.1 mu/l	(1-10)
FSH	1.4 mu/l	(1-10)
Cortisol (pre-synacthen)	88 nmol/l	(220 – 800)
Cortisol (post-synacthen)	180 nmol/l	(220 – 800)

Which of the following is most likely the diagnosis?

- **A)** Factitious results
- **B)** Lymphocytic hypophysitis
- **C)** Non-functional pituitary tumour
- **D)** Postpartum thyroiditis
- **E)** Sheehan syndrome

Answer

Correct answer : Lymphocytic hypophysitis

The patient appears to have a pan-hypopituitarism and the likely diagnosis is a lymphocytic hypophysitis, as there is no evidence of Sheehan's syndrome (pituitary infarction following obstetric haemorrhage). The patient is unlikely to have a non-functional pituitary tumour as, we are told, she had no problems with conception or pregnancy. Previously, many of the patients who had been considered to have Sheehan's syndrome probably had lymphocytic hypophysitis.

Question 27

A 35 year old female presents with a six month history of headaches, oligomenorrhoea and galactorrhoea. She describes episodic, 'bad' headaches which affect the left eye and left frontal region, are associated with lacrimation of the left eye and also some injection of that eye. These episodes typically last 10-15 mins with little relief from analgesia such as paracetamol. The headaches often occur with a frequency of 2-5 episodes daily.
Her GP has undertaken some blood tests which reveal an elevated prolactin of 3500 mu/l and a CT scan revealed a pituitary intrasellar adenoma of approximately 0.9 cm. On examination there is little note other than she has a BMI of < 30 kg/m^2, and some galactorrhoea to expression but otherwise visual fields, acuity and fundal examination are normal
Which of the following is the likely explanation of the headaches associated with her pituitary tumour?

- **A)** Benign intracranial hypertension
- **B)** Cluster headaches
- **C)** Migraine
- **D)** Paroxysmal hemicrania
- **E)** Trigeminal neuralgia

Answer

Correct answer : Paroxysmal hemicrania

This is a classical description of paroxysmal hemicrania, a distinct type of headache described in conjunction with pituitary tumours. A further revision of this headache is termed short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT). The aetiology of such headaches is unknown but may relate to neurohormonal effects or in some circumstances where the tumour is larger, to pressure effects of the tumour on the cavernous sinus trigeminal nerve. The importance of recognising this headache is that it responds well to treatment with indomethacin. In functional adenomas such as prolactinomas, reports suggest that it may respond or indeed develop/deteriorate following dopamine agonist therapy.

Question 28

A 62 year old woman is referred with persistent hypertension and obesity. She also complains of excessive pigmentation and headaches. 30 years ago she was diagnosed with Cushing's disease and underwent a bilateral adrenalectomy. She is treated with hydrocortisone 10 mg bd and fludrocortisone 100 micrograms daily and also receives amlodipine and atenolol as long standing treatment of the hypertension

On examination, she is noted to be generally pigmented, has abdominal striae and blood pressure is 168/100 mmHg. Visual fields are full to confrontation.

Which of the following is the most appropriate investigation for this patient?

- **A)** 24-hour urinary free cortisol measurement
- **B)** ACTH concentration
- **C)** Aldosterone:plasma renin ratio
- **D)** Renal ultrasound with dopplers of renal arteries
- **E)** Short synacthen test

Answer

Correct answer : ACTH concentration

Nelson's syndrome occurs in roughly 30% of patients who have undergone adrenalectomy for pituitary-dependent Cushing's disease. It is a consequence of the clinical progression of any pre-existent pituitary adenoma possibly after the feedback of hypercortisolism has been removed by adrenalectomy. Plasma ACTH levels are markedly elevated and pituitary imaging is likely to reveal an adenoma. Pituitary irradiation is frequently performed early after adrenalectomy in Cushing's disease in order to avert Nelson's disease.

Question 29

A 52 year old female is admitted with an intracranial bleed. She undergoes clipping of a cerebral arterial aneurysm and is well the following morning. The following biochemistry are noted postoperatively: (Normal ranges Sodium 135-145, potassium 3.5 -5, Urea 3-8, Creatinine 50-100)

Day 1	Plasma Sodium 131 mmol/l	Potassium 3.6 mmol/l	Urea 4.5 mmol/l	Creatinine 95 µmol/L
Day 2	Plasma Sodium 126 mmol/L	Potassium 3.4 mmol/L	Urea 4.2 mmol/L	Creatinine 88 µmol/L
Day 3	Plasma Sodium 123 mmol/L	Potassium 3.5 mmol/L	Urea 5 mmol/L	Creatinine 88 µmol/L
Day 4	Plasma sodium 120 mmol/L	Potassium 3.5 mmol/L	Urea 5 mmol/L	Creatinine 88 µmol/L

On day 4 she was commenced on a fluid restriction of 1 litre per day. The following were noted at that stage: Plasma osmolality 258 mosmol/l (275-305) urine osmolality 688 mosmol/l with urine sodium 84 mmol/l.
Which of the following is the most likely diagnosis to explain the hyponatraemia?

- **A)** Cranial diabetes insipidus
- **B)** Hypoadrenalism
- **C)** Fluid overload
- **D)** Syndrome of inappropriate ADH (SIADH)
- **E)** Sick cell syndrome

Answer

Correct answer : Syndrome of inappropriate ADH (SIADH)

This patient has a deteriorating hyponatraemia with an inappropriately elevated urine osmolality and urine sodium excretion (should be less than 20 mmol/l). The most likely diagnosis is therefore SIADH. There is no evidence of hypoadrenalism. Diabetes insipidus would produce excessive fluid loss with hypernatraemia. Fluid overload is a potential diagnosis yet we are informed that the patient underwent fluid restriction.

Question 30

A 38 year old female presents with tiredness, lethargy and weight gain. Five years previously she had undergone trans-sphenoidal hypophysectomy for a non-functional pituitary tumour. She had a complicated post operative course having developed a cerebrospinal fluid leak which required re-exploration and then seizures for which she remains on sodium valproate. She was demonstrated to be hypopituitary for which she receives hydrocortisone 10 mg bd, thyroxine 100 micrograms/d and combined HRT. You suspect that a growth hormone deficiency is likely to be responsible for her current symptoms.
Which of the following investigations would be the most appropriate test to confirm growth hormone deficiency in this patient?

- **A)** Clonidine test
- **B)** Combined GHRH/Arginine test
- **C)** IGF-1 concentration
- **D)** Insulin tolerance test
- **E)** Oral glucose tolerance test

Answer

Correct answer : IGF-1 concentration

This patient already has three hormone deficiencies and hence only needs testing of IGF-1 levels to confirm GHD as GH is typically the first pituitary hormone to be lost in hypopituitarism. If suboptimal GH therapy can be considered.

Question 31

A 16 year old is reviewed in the endocrinology transition clinic. He was diagnosed to have a craniopharyngioma at the age of 14 and operated upon. Post operatively, he is lagging behind his peers as far as his height is concerned (2 standard deviation below normal). Both of his parents are of average height and none of his siblings has short stature. His biochemical profile is as shown below:

		Normal Ranges
9 am cortisol	320 nmol/L	
30 minutes Post ACTH	580 nmol/L	
FSH	10.4 U/L	(1.4-18.1 U/L)
LH	5.5 U/L	(3.0-8.0 U/L)
IGF-1	12 nmol/L	(16-118 nmol/L)
Prolactin	92 mU/L	(45-375 mU/L)
Testosterone	11.2 nmol/L	
TSH	2.2 mU/L	(0.35-5.5 mU/L)

Subsequently an insulin stress test is arranged for him in the endocrine day unit which shows a peak growth hormone value of 8 mU/L. What is the most useful advice as far as growth hormone (GH) replacement is concerned?

- **A)** GH replacement is contraindicated considering his history of tumour
- **B)** No need to replace him with GH therapy based on these results
- **C)** Start him on an adult dose of GH replacement and monitor IGF-1 levels
- **D)** Start him on GH replacement if he scores > 12 on AGHDA
- **E)** Start him on a paediatric dose of GH replacement

Answer

Correct answer : Start him on an adult dose of GH replacement and monitor IGF-1 levels

This 16 year old clearly has GH deficiency as a post-operative complication of craniopharyngioma resection. He will require 0.15-0.3 mg daily subcutaneous GH injections and the dose titration is based on IGF-1 levels (to a maximum of 1 mg/day). The main side effects associated with GH injections include fluid retention, myalgia, arthralgia and benign intracranial hypertension. It is contraindicated in the presence of any active malignancy in the body.

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Question 32

A 29 year old, who had undergone resection of a 2.5 cm nonfunctioning pituitary tumour 2 years ago, presents to the clinic with low mood and non-specific symptoms. He has a background history of epilepsy for which he is currently taking Levetiracetam.
His initial screening reveals normal FSH/LH/TFT/Prolactin/Testosterone concentrations. A short synacthen test shows 30 minute cortisol value of 620 nmol/L. His IGF-1 level is 20.5 nmol/L (25-45). Which of the following tests should be employed for this patient?

- **A)** Clonidine test
- **B)** Glucagon stimulation test
- **C)** Glucose tolerance test
- **D)** IGFBP3 levels
- **E)** Insulin tolerance test

Answer

Correct answer : Glucagon stimulation test

The gold standard for the diagnosis of GH secretion is the insulin tolerance test (ITT). GH levels of <3 µg/L (<10 mU/L) are usually indicative of severe GH deficiency on ITT. The contraindications for ITT include a history of epilepsy, ischaemic heart disease and basal cortisol levels < 100 nmol/L. ITT is contraindicated in this patient as he is an epileptic evidenced by the levariactem therapy he is receiving. The GHRH-Arginine test is also highly sensitive as well as specific to detect GH deficiency and would have been an ideal choice as an alternative to ITT in this patient, if this choice was provided as an answer. Glucagon stimulation testing can also be used for GH deficiency assessment if ITT is contraindicated.

Question 33

A 27 year old lady, who delivered a healthy baby girl 3 months back, by a normal vaginal delivery, presents with a 2 weeks history of headache and visual blurring. Her biochemistry results are shown below:

		Normal Ranges
Sodium	126 mmol/L	(135-145 mmol/L)
Potassium	3.8 mmol/L	(3.5-5.5 mmol/L)
Urea	8.5 mg/dL	(7-20 mg/dL)
Creatinine	105 µmol/L	(60-115 µmol/L)
Calcium	2.4 mmol/L	(2.2-2.6 mmol/L)
TSH	2.4 mU/L	(0.35-5.5 mU/L)
Free T4	8.5 pmol/L	(11.5-22.7 pmol/L)
Prolactin	550 mU/L	(50-500)
Glucose	6.3 mmol/L	(3.5-5.5)

MRI images show an enlarged pituitary gland. What is the likely underlying diagnosis?

- **A)** Lymphocytic hypophysitis
- **B)** Macroprolactinoma
- **C)** Non functioning pituitary adenoma
- **D)** Sheehans syndrome
- **E)** SIADH

Answer

Correct answer : Lymphocytic hypophysitis

Lymphocytic hypophysitis is a rare infiltrative disorder leading to anterior pituitary destruction during late pregnancy or in the postpartum period. It usually presents with symptoms of mass effect including headache, nausea and vomiting. Deficiency of ACTH and TSH hormones is more commonly observed as compared to GH/ gonadotropin deficiency. MRI shows an enlarged mass with thickening of the pituitary stalk. Treatment includes replacement of the deficient anterior pituitary hormone. The role of steroid replacement in lymphocytic hypophysitis remains unproven.

Question 34

A 65 year old male with an inoperable ACTH-secreting pituitary adenoma, undergoes bilateral adrenalectomy. The follow up for this gentleman should include which the following investigations?

- **A)** 17 OH progesterone measurement
- **B)** Basal and 1 hour post steroid dose ACTH levels
- **C)** Calcitonin
- **D)** Cortisol levels
- **E)** Urea and electrolytes

Answer

Correct answer : Basal and 1 hour post steroid dose ACTH levels

Bilateral adrenalectomy is still occasionally employed in patients with inoperable pituitary adenoma. These patients have about a 50% risk of development of Nelson's syndrome after 10 years of operation as a result of increased ACTH levels (due to a loss of feedback inhibition). The incidence can be reduced if the pituitary gland is subjected to preoperative radiotherapy. After bilateral adrenalectomy annual monitoring is usually recommended by measurement of basal and 1 hour post steroid dose ACTH levels and yearly MRI scans.

Question 35

A 54 year old male with acromegaly and treated unsuccessfully with a trans-sphenoidal resection of a tumour, is currently receiving pegvisomant in view of his residual disease. His blood results are as shown:

		Normal Ranges
IGF-1	12 nmol/L	(10-35 nmol/L)
GH	44 mU/L	(0-20 mU/L)
Prolactin	250 mU/L	(45-375 mU/L)

What is the likely advice you will give?

- **A)** Continue the same dose of pegvisomant
- **B)** Decrease the dose
- **C)** Repeat radiotherapy
- **D)** Start him on octreotide
- **E)** Stop pegvisomant

Answer

Correct answer : Continue the same dose of pegvisomant

Pegvisomant is a genetically modified analogue of growth hormone which acts as a highly selective growth hormone receptor antagonist. It is licensed for treatment of patients with acromegaly who have undergone incomplete/ inadequate surgical resection and are unresponsive to somatostatin analogue therapy. It leads to normalisation of IGF-1 levels in more than 90% of patients although the growth hormone level need to be monitored as it may show an increase.

Usage of pegvisomant is limited due to the high cost of therapy. The above mentioned patient is showing good response to pegvisomant therapy as reflected by normalisation of IGF-1 levels so the therapy should be continued at the same dose with regular monitoring of liver function tests.

Question 36

A 26 year old is referred to endocrinology clinic with a 3 months history of amenorrhoea (but no galactorrhoea) due to a suspected microprolactinoma. Her investigations show:

		Normal Ranges
Prolactin levels	1804 mU/L	(60-620)
Oestradiol	1025 pmol/L	(130-1000)
FSH	0.1 mu/l	(1-10)
LH	0.2 mu/l	(1-10)

What is the most likely underlying diagnosis?

- **A)** CAH
- **B)** Hypothyroidism
- **C)** Microprolactinoma
- **D)** Oestradiol secreting ovarian tumour
- **E)** Pregnancy

Answer

Correct answer : Pregnancy

Presence of a 3 month history of secondary amenorrhoea, elevated oestrogen levels, and suppressed FSH/LH levels with elevated prolactin levels in a female in reproductive age group is consistent with a pregnant state and needs further confirmation with an urinary pregnancy test / ultrasonography.

Question 37

A 28 year old female who is 35 weeks pregnant presents with a worsening headache and visual loss. She has a history of macroprolactinoma for which she originally took cabergoline but has not taken any medications since she discovered she was pregnant. Urgent MRI reveals an increase in the size of the macroprolactinoma with compression of the optic chiasm. Which is the most appropriate next step in her management?

- **A)** Octreotide infusion
- **B)** Radiotherapy
- **C)** Refer to neurosurgery for removal of tumour
- **D)** Re-commence dopamine agonist therapy
- **E)** Urgent caesarean section

Answer

Correct answer : Re-commence dopamine agonist therapy

The risk of a significant growth in size of a macroprolactinoma is about 25% (as compared to 1-2% in patients with a microprolactinoms). Therefore, patients with a macroprolactinoma should be closely monitored during pregnancy with clinical examination and formal visual field assessment. An increase in size of the lesion warrants initiation of dopamine agonist therapy. Alternatively patients with macroprolactinoms can either undergo surgical debulking of the tumour before conception or dopamine agonist therapy can be continued throughout the pregnancy.

Question 38

A 26 year old male is referred by the GP who queries a diagnosis of acromegaly. His symptoms include headaches, sweats and he has noticed enlargement of the hands and feet. He informs you that he has a cousin who has been diagnosed with a pituitary tumour and his father died of acromegaly many years ago. He is a non-smoker and has otherwise been well. On examination he has a slight acromegalic appearance and his investigations reveal:

		Normal Ranges
IGF -1	112 nmol/l (30-55)	
GH response to OGTT	5.5 mcg/l (<1)	

Regarding any potential genetic screening, which of the following would be the most appropriate?

- **A)** AIP mutations
- **B)** MEN type 1 mutations
- **C)** No genetic screening required
- **D)** SDHD type B or D mutations
- **E)** vHL gene deletion

Answer

Correct answer : AIP mutations

This patient presents with a convincing history of hereditary pituitary tumours. In particular, familial acromegaly has been associated with a mutation of the aryl-hydrocarbon receptor interactive protein (AIP) within the 11q13 region. The mechanism underlying this propensity to pituitary tumour formation is unknown but recognition of the diagnosis is important in the identification of at risk kindreds.

Question 39

A 55-year-old man attends clinic. He has been diagnosed with a prolactinoma and is receiving treatment with cabergoline 5mg twice weekly. His original prolactin concentration was 30,000 mu/l (<450) and his most recent concentration on this cabergoline dose escalated over the last year is 18,000 mu/l. Originally his visual fields were normal and there is no abnormality on confrontation today. The original MRI reveals that the tumour was at the optic chiasm but not compressing it, within extension into the cavernous sinus. A repeat MRI has shown that there has been a slight reduction in the size of the tumour which is abutting but not compressing the optic chiasm. He is also receiving testosterone IM and thyroxine.
Which of the following would be the most appropriate approach to the management of this patient?

- **A)** Advise pituitary surgery
- **B)** Advise stereotactic radiosurgery
- **C)** Continue on the same dose of cabergoline
- **D)** Increase the dose of cabergoline to 6 mg twice weekly
- **E)** Switch cabergoline to quinagolide

Answer

Correct answer : Advise pituitary surgery

This patient has dopamine agonist resistance and is on maximal cabergoline therapy. Evidence suggests that cabergoline is the most effective dopamine agonist in the management of prolactinomas and there would be little to gain from switching to an alternative agent. Whilst there has been some minor shrinkage of the tumour, Prl concentrations are still not controlled and, with the tumour abutting the chiasm, surgery would be most appropriate. Radiotherapy/radiosurgery would not be advised in this large prolactinoma close to the chiasm, as even with radiosurgery, the chiasm would still be in the radiation field.

Question 40

You see a 35-year-old man in clinic with ‘congenital hypopituitarism’, diagnosed when he was 5 due to growth failure. He is generally well and has no problems. The patient is taking thyroxine, testosterone and growth hormone. Mutation of which of the following is the likely cause of this man’s hypopituitarism?

- **A)** AIP
- **B)** HESX1
- **C)** Pit-1
- **D)** Prop-1
- **E)** SDH-type b

Answer

Correct answer : Prop-1

The most probable cause of this man’s congenital hypopituitarism is inactivating mutation of the Prop-1 gene, which typically causes GH, LH/FSH, TSH and occasionally ACTH deficiency. The disorder is diagnosed from 9 months to 8 years of age. This contrasts with Pit-1 which causes deficiencies of prolactin, GH and TSH.

PROP1-Related Combined Pituitary Hormone Deficiency

Heritable Disorders of Pituitary Development

Question 41

A 45-year-old man is being treated for hypopituitarism which is a consequence of treatment of a non-functioning pituitary tumour. He attends clinic complaining of fatigue. He is on full replacement therapy except growth hormone. His investigations confirm GH deficiency and his AGHDA score as measured on the questionnaire is 20/25. He is treated for 9 months with GH therapy at a dose of 0.5 mg/d. His IGF-1 is 23.3 nmol/L (normal age adjusted range 15-28). His AGHDA score is 14. Which of the following is the most appropriate approach with regard to his GH therapy?

- **A)** Continue GH at current dose
- **B)** Continue on a dose of 0.4mg GH daily
- **C)** Increase dose of GH to 0.6 mg daily and review AGHDA score/IGF-1 in 3 months
- **D)** Increase dose of GH to 0.7 mg daily and review AGHDA/IGF-1 in 3 months
- **E)** Stop GH

Answer

Correct answer : Stop GH

There are specific NICE criteria for GH therapy and, in this patient whose IGF-1 is in the upper half of the age related normal range (and is thus on adequate replacement), the patient has only managed an improvement of 6 points on AGHDA. NICE stipulate that an improvement in AGHDA score of 7 or above is required to merit continued GH treatment.

Review of TA64; Human growth hormone (somatropin) in adults with growth hormone deficiency

Question 42

A 17-year-old female attends clinic with a 9 month history of galactorrhoea. She is taking the oral contraceptive and has regular withdrawal bleeds. Her prolactin is measured at 15000 mu/l (<450) and MRI of the pituitary reveals a 1.5 cm macroadenoma which extends into the suprasellar cistern but is not touching the chiasm. There is no family history of endocrine disease of note.

You elect to treat her with cabergoline commencing at 0.25 mg twice weekly. Which of the following genetic analysis would you also request?

- **A)** AIP gene
- **B)** GS alpha mutation
- **C)** MEN-1 gene
- **D)** No specific genetic test appropriate
- **E)** Prop-1 gene

Answer

Correct answer : AIP gene

This young woman has a prolactinoma and studies reveal that such patients should be tested for AIP-related family pituitary adenomas. It is an autosomal dominant condition though the majority are spontaneous mutations. However, detection of the genetic defect is important for screening of siblings and also for offspring. Individuals that develop a somatotroph or lactotroph adenoma below the age of 30 should be screened for AIP.

AIP-Related Familial Isolated Pituitary Adenomas

Question 43

A 32-year-old woman has been treated for a microprolactinoma with cabergoline 0.25 mg twice weekly. She has received 2 years of treatment and has had regular menses. The most recent prolactin concentration is 70 mu/l (<450). She is tolerating treatment well.
Which of the following would be the most appropriate approach to the continued management of this patient?

- **A)** Arrange echocardiography
- **B)** Arrange MRI of pituitary
- **C)** Increase dose of cabergoline
- **D)** Reduce dose of cabergoline
- **E)** Therapeutic withdrawal

Answer

Correct answer : Therapeutic withdrawal

This woman has had 2 years of treatment with a dopamine agonist for a microprolactinoma. The evidence suggests that one can try a therapeutic withdrawal of the cabergoline and that roughly 40% of such patients will remain in remission. There is no requirement for an echo if one is embarking on a therapeutic withdrawal and the endocrine society now advocate that with such small doses of DA that echo is no longer required.

There is no need to repeat a MRI if the prolactin is appropriately suppressed as the control of the prolactin reflects control of the microprolactinoma.

Medscape

Question 44

A 24-year-old woman presents with a three month history of thirst and polyuria. She has no other medical history of note other than taking the combined oral contraceptive. You arrange a water deprivation test which reveals the following:
Start test 9am

	Urine volume mls	Urine osmolality mosmol/l	Weight kg	Plasma osmolality mosmol/l
9.30am	350	100	88.2	275
11am	200	150		
12.30	240	160		
2pm	350	180		
3.30pm	220	170	88	285
End of test 4pm Total	**1360**			

Which of the following is the correct interpretation of the results?

- **A)** Cranial diabetes insipidus
- **B)** Nephrogenic diabetes insipidus
- **C)** Partial diabetes insipidus
- **D)** Primary polydipsia
- **E)** Surreptitious fluid intake

Answer

Correct answer : Surreptitious fluid intake

The water deprivation test is a useful investigation of polyuria and polydipsia. You'll need to know how to interpret test results accurately. It is an 8 hour test whereby the patient is allowed to drink ad libitum until the start of the test and then the urine volume osmolality are checked. Weight is also measured throughout the test. Normal results of the water deprivation test would reveal a decline in urine volumes and increasing urine osmolality (typically twice that of plasma osmolality). The patient is not permitted to drink during the test.

In this case, we see that there is a volume loss of 1360 mls equivalent to 1.36 kg of fluid loss. Yet, there has only been a weight change of 200 g. This is impossible unless the patient has been drinking surreptitiously during the test. This also explains why the plasma osmolality hasn't changed that much during the test. This is the most appropriate answer rather than primary polydipsia as it means that confirming the diagnosis of the latter requires the test to be arranged with adequate patient supervision.

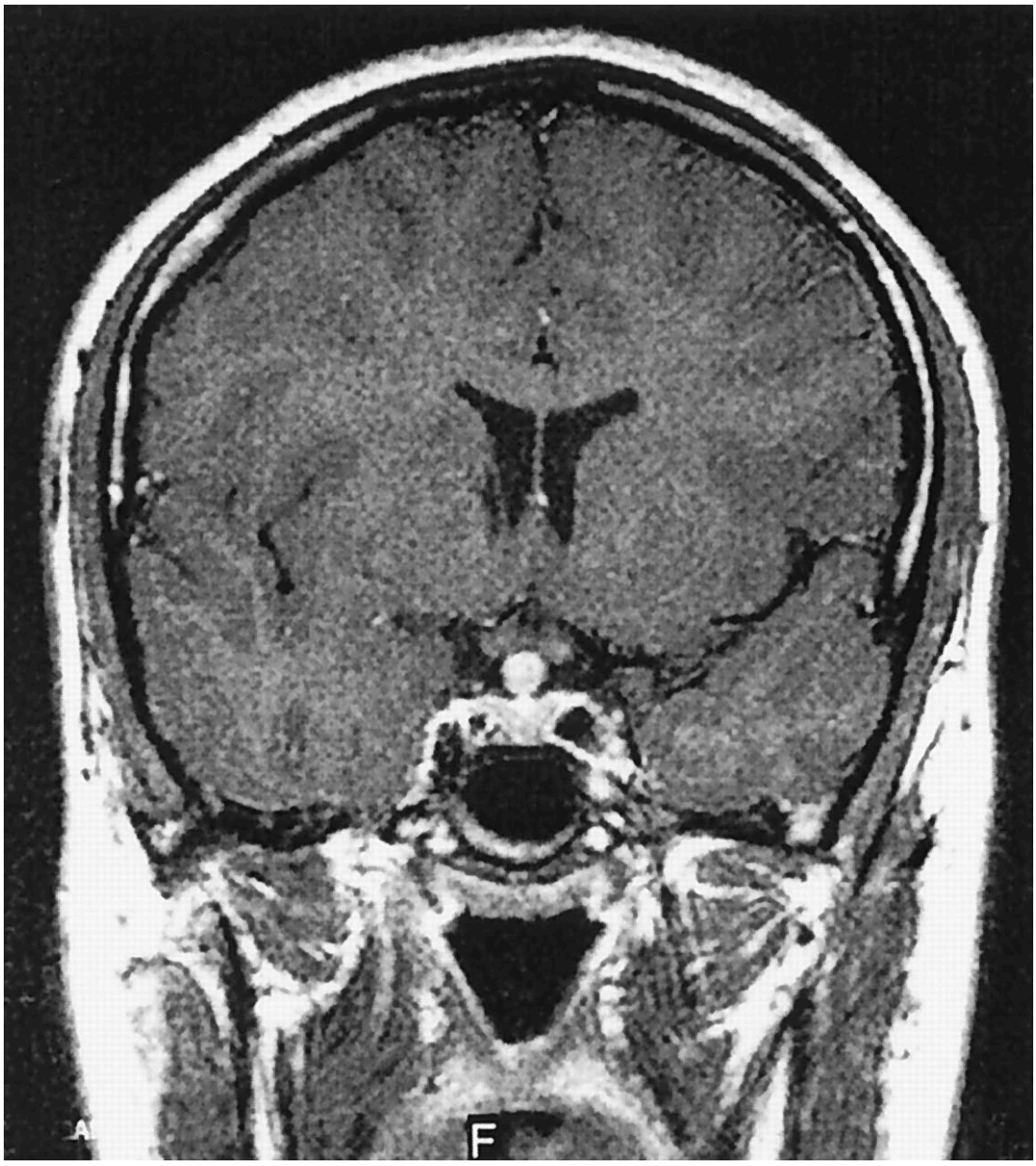
Wass, J., 2008. How to do a water deprivation test: interpretation of results.

Question 45

A 41-year-old woman presents with fatigue, weight loss and polyuria/polydipsia. She is getting up 4-5 times per night to pass urine. She also describes a 4-month history of amenorrhoea. Investigations reveal the following:

		Normal Ranges
T4	8 pmol/l	(9-23)
TSH	1.1 mu/l	(0.5-5)
SST 30 min Cortisol	320 nmol/l	(>450)
Prolactin	1100 mu/l	(50-450)

The MRI of the pituitary is shown



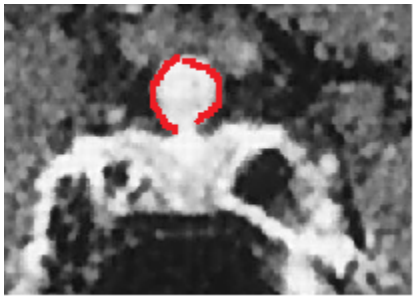
Which of the following is a possible explanation for the presentation and results?

- **A)** Hypothalamic glioma
- **B)** Lymphocytic hypophysitis
- **C)** Non-functional pituitary tumour with stalk compression
- **D)** Prolactinoma
- **E)** Rathke’s cyst

Answer

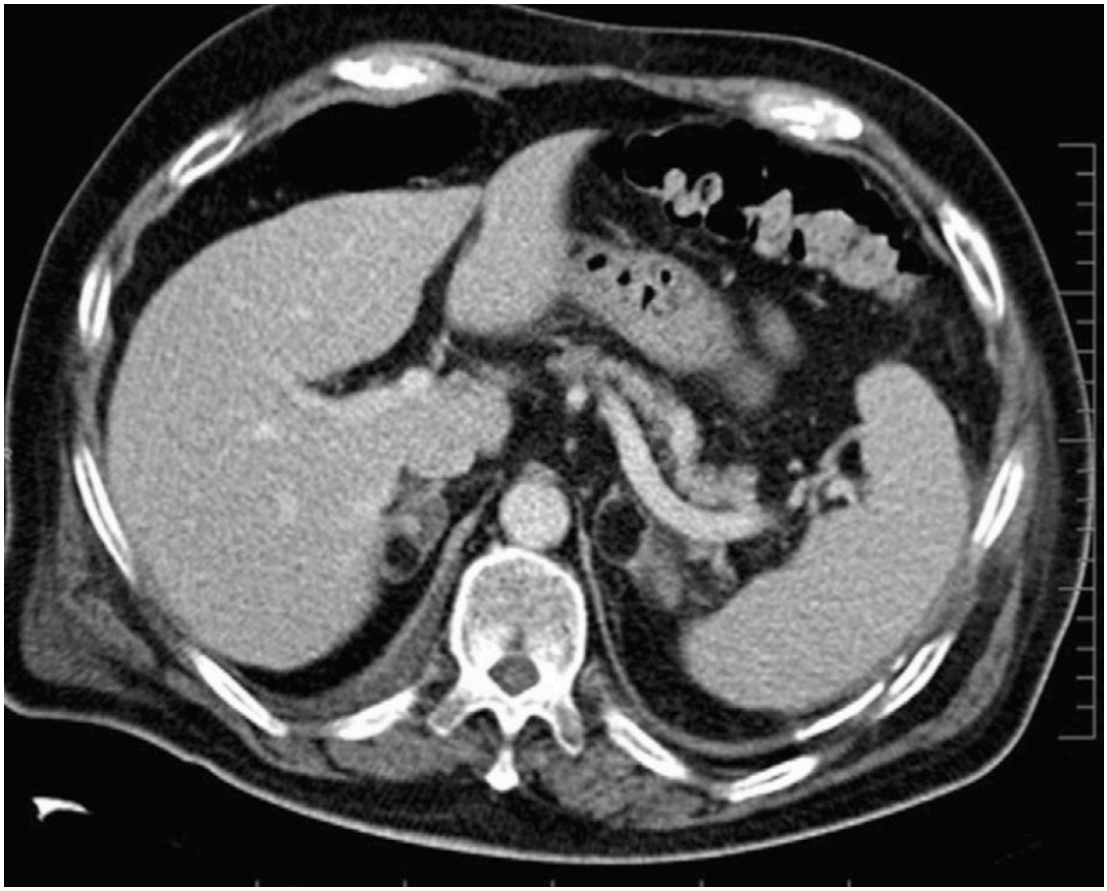
Correct answer : Lymphocytic hypophysitis

This woman has pan-hypopituitarism and is likely to have diabetes insipidus according to the history. Posterior pituitary dysfunction with DI is unusual in association with anterior pituitary tumours. In this case the MRI reveals a pituitary stalk mass (red) and the potential unifying diagnoses would be neurosarcoidosis, lymphocytic hypophysitis, germinoma and histiocytosis. Although a little grainy, the rest of the pituitary does not appear abnormal on this film.



Question 46

A 54-year-old man has had a CT scan of his abdomen as an investigation of abdominal pain with change of bowel habit.



What is shown in this CT?

- **A)** Bilateral adrenal adenomas
- **B)** Left adrenal lesion
- **C)** Numerous hepatic metastases likely carcinoid
- **D)** Pancreatic tumour
- **E)** Right adrenal adenoma

Answer

Correct answer : Bilateral adrenal adenomas

Like many of the patients we see referred to endocrinology, this patient has had a CT scan for some abdominal reason which shows up adrenal lesions. About 5% of abdo scans will reveal adrenal lesions. In this case, the bilateral adrenal lesions (red) are likely to be myeolipomas, as their characteristics are black, matching the intra-adbominal fat, making them highly fat rich i.e myolipomas rather than adenomas. Hounsfield units are useful in determining the density of an adrenal adenoma, with 10Hu or below suggesting an adenoma.

Further Reading:

1. Adrenals Differentiating benign from malignant Theo Falke and Robin Smithuis

Question 47

A 19-year-old girl re-presents with recurrent Cushing's disease (CD). She was originally diagnosed with Cushing's by the paediatricians at the age of 15. She underwent surgical resection of a microadenoma, had a post-operative cortisol of 32 nmol/l (120-400) and did well for 2 years before the symptoms and characteristic features returned. Previous histology confirmed an adrenocorticotropic hormone (ACTH) secreting microadenoma. She was left eupituitary after microadenomectomy. Repeat MRI reveals a further microadenoma on the right side of the gland and testing confirms recurrent Cushing's with an ACTH of 33 pmol/l (10-50). All other pituitary profiles are normal.

Which further investigation prior to pituitary surgery would you request for this patient?

- **A)** Blood calcium levels
- **B)** Inferior petrosal sinus sampling
- **C)** Pancreatic MRI
- **D)** Whole body PET
- **E)** CRF concentrations

Answer

Correct answer : Blood calcium levels

This is a really tough question and tests really high end endocrine skills. It is very unusual for a youngster to have Cushing's disease and even more unusual for the patient to have an effective 'cure' as illustrated by the post-op cortisol of less than 50 pmol/l, only for recurrent Cushing's disease to return so swiftly. The age and the recurrent disease would suggest an underlying genetic abnormality such as MEN Type 1 and the most appropriate investigation would be measurement of calcium levels. Often mutations are sporadic and the family history may be uneventful. Primary hyperparathyroidism is typically the earliest manifestation of MEN type 1 with all patients presenting before 30 years of age. Multiple pituitary adenomas are more prevalent with MEN type 1 than sporadic CD.

This is Cushing's disease rather than ectopic Cushing's as suggested by the original diagnosis with a microadenoma and the ACTH of 32 again suggesting CD.

Simonds, W.F., Varghese, S., Marx, S.J. and Nieman, L.K., 2012. Cushing's syndrome in multiple endocrine neoplasia type 1. Clinical endocrinology, 76(3), pp.379-386.

Question 48

A 45-year-old male is diagnosed with a macroprolactinoma with a prolactin of 42,000 mu/l (<450). He is treated with cabergoline with dose escalation and his prolactin concentration declines to 1500 mu/l but over time begins to rise. On a dose of 5 mg of cabergoline twice weekly, his prolactin is 35,000 mu/l. Serial scanning reveals original reduction in the size of the macroprolactinoma with gradual expansion and the tumour touches but does not compress the optic chiasm. He undergoes pituitary resection and his post-operative prolactin is 133 mu/l. Post-operative MRI reveals substantial resection of the tumour. Histology confirms a lactotroph pituitary tumour with a Ki 67 index of 30-40% (<5%).

Which of the following is the most appropriate approach to the further management of this patient?

- **A)** Fractionated radiotherapy
- **B)** No further treatment required at this stage. Monitor with serial prolactin
- **C)** Restart cabergoline
- **D)** Temozolomide

Answer

Correct answer : Fractionated radiotherapy

There has been substantial resection of this dopamine agonist resistant macroprolactinoma with surgical ‘cure’. The Ki67 antigen provides a reflection of the proliferation and invasiveness of tumours and in this case is very high, suggesting that this is a particularly aggressive prolactinoma. Despite the complete resection, there would be a high chance of tumour recurrence and the patient should be offered fractionated radiotherapy.

Gürlek, A., Karavitaki, N., Ansorge, O. and Wass, J.A., 2007. What are the markers of aggressiveness in prolactinomas? Changes in cell biology, extracellular matrix components, angiogenesis and genetics. European Journal of Endocrinology, 156(2), pp.143-153.

Question 49

A 40-year-old woman has been referred to the endocrine clinic with symptoms of polyuria and polydipsia. She has been drinking 4 litres of water at least, daily. She has nocturia and gets up about 3 to 4 times at night to pass urine. She has a past medical history of dysmenorrhoea and she occasionally takes NSAIDS. She is a non-smoker and does not drink alcohol. She was an adoptive child and lost contact with her family. Her body weight is 60 Kg. Her general and systemic examination is normal. Her blood results show:

		Normal Ranges
Sodium	142 mmol/L	(133-146)
Potassium	4.1 mmol/L	(3.5-5.3)
Urea	3.9 mmol/L	(3-8)
Creatinine	69 umol/	(50-100)
HbA1c (IFCC traceable)	32 mmol/mol	(<48)
Calcium (adjusted)	2.27 mmol/L	(2.2-2.6)
Osmolality [Urine]	207 mmol/Kg	
Sodium [Urine]	<20 mmol/L	

She then underwent a water deprivation test and the results are as follows:

Urine osmolality	mmol/kg
0 hours	189
2 hours	339
4 hours	526
6 hours	801

During the test she lost about 0.9kgs in weight. Plasma osmolality at the start and end of the test were 297 mmol/l and 298 mmol/L respectively. What is the most likely diagnosis?

- **A)** Cranial diabetes inspidus
- **B)** Drug induced polydipsia

- **C)** Nephrogenic diabetes insipidus
- **D)** Partial polydipsia
- **E)** Primary polydipsia

Answer

Correct answer : Primary polydipsia

Explanation:

This patient has got primary polydipsia. On the water deprivation test, she had an appropriate rise in urine osmolality with time. Primary polydipsia (sometimes called psychogenic polydipsia) is characterized by a primary increase in water intake. This disorder is most often seen in middle-aged women and in patients with psychiatric illnesses, including those taking antipsychotics. Primary polydipsia can also be induced by hypothalamic lesions that directly affect the thirst centre, as may occur with an infiltrative disease such as sarcoidosis.

Rose, B.D., 1977. Clinical physiology of acid-base and electrolyte disorders. McGraw-Hill. New York 2001. p.748, 767

Question 50

A 68-year old woman with allergic bronchopulmonary aspergillosis (ABPA) and asthma presented to endocrine clinic with a 2 week history of increasing tiredness and shortness of breath. She denied headache, visual disturbance, nausea, vomiting or collapse. Her medication included Seretide 250 Evohaler (fluticasone 250 mcg and salmeterol 25 mcg) one puff twice daily for four years and inhaled salbutamol. She had been treated with itraconazole 200 mg OD for two years with unsuccessful attempts to stop this medication due to recurrence of the disease. She had never required treatment with oral corticosteroids.
On examination, her observations were stable with no postural hypotension. Her physical examination was normal and she had no features of endocrinopathy.
Full blood count, renal and liver function tests were within normal limits. Her pituitary profile TSH, FSH, LH, prolactin and IGF-1 results were within age specific normal limits.

	Results	Normal Range
Cortisol at 09:00 hours	30 nmol/l	138-635 nmol/l
Adrenocorticotropic hormone (ACTH)	8.1 pg/ml	7–51 pg/ml
Adrenal autoantibodies	negative	-

Chest X ray and MRI pituitary showed no abnormal findings.
What is the most likely diagnosis?

- **A)** Addison’s disease
- **B)** Drug induced adrenal insufficiency
- **C)** Lymphocytic hypophysitis
- **D)** Non-functioning pituitary adenoma
- **E)** Pituitary histiocytosis

Answer

Correct answer : Drug induced adrenal insufficiency

Explanation:

The likely cause of this condition is due to a pharmacological interaction between inhaled fluticasone and oral itraconazole causing hypothalamic-pituitary-adrenal (HPA) axis suppression. This interaction had been well described in the literature. Itraconazole is a potent inhibitor of cytochrome P450 dependent CYP3A4 and thereby decreases the metabolic clearance of synthetic glucocorticoids. This, in turn causes an increase in corticosteroid levels which negatively feedbacks on the HPA axis causing adrenal insufficiency.

Reference:

- Gilchrist, F.J., Cox, K.J., Rowe, R., Horsley, A., Webb, A.K., Jones, A.M. and Bright-Thomas, R.J., 2013. Itraconazole and inhaled fluticasone causing hypothalamic–pituitary–adrenal axis suppression in adults with cystic fibrosis. Journal of Cystic Fibrosis, 12(4), pp.399-402

Question 51

A 45-year-old man is diagnosed with acromegaly by the endocrinologists. The patient has the classical appearances of acromegaly but has no skin tags or acanthosis nigricans. He denies any bowel symptoms. His IGF-1 concentration is 112 nmol/l (NR 10-40). MRI confirms a pituitary adenoma and he is scheduled for pituitary surgery. His investigations including FBC, U+Es, Calcium and TFTs are normal.

Which of the following should be undertaken regarding colonoscopic screening for this patient?

- **A)** Colonoscopic screening should be performed at diagnosis
- **B)** Colonoscopic screening should be performed at diagnosis and annually even if patients are cured of acromegaly
- **C)** Colonoscopic screening should only be performed if the patient is not cured by surgery and/or medical therapy
- **D)** Colonoscopy is not the most appropriate approach for screening due to technical difficulties and CT colonoscopy is most appropriate
- **E)** No colonoscopic screening is required in acromegaly

Answer

Correct answer : Colonoscopic screening should be performed at diagnosis

Explanation

Due to the higher risk of colonic adenomatous polyps and therefore the risk of cancer, guidelines suggest that all acromegalics should have an initial colonoscopic screening performed in individuals at or above age 40. The frequency of screening then depends on the original findings at diagnosis together with disease activity. Those with a polyp at initial screening or with elevated IGF-1 require screening every 3 years whilst those clear at initial screening can have 5 -10 year colonoscopic follow up.

Reference

- Screening guidelines for colorectal cancer and polyps in patients with acromegaly

Question 52

A 48-year-old patient with a diagnosis of acromegaly treated with surgery had a screening colonoscopy recently which revealed 4 small adenomatous polyps removed. Following surgery he was considered to be in remission and his most recent IGF-1 was 12 nmol/l (9 - 25). When will he be due for his next surveillance colonoscopy?

- **A)** 1 year
- **B)** 18 months
- **C)** 2 years
- **D)** 3 years
- **E)** 5 years

Answer

Correct answer : 3 years

Explanation:

Patients with acromegaly are at increased risk of developing colorectal cancer. Specific colorectal screening is required which differs from other colorectal cancer screening. Colonoscopic screening should start at the age of 40 years unless there are colonic symptoms at an earlier age. In this case with the adenoma present it should be 3 -5 years and one would probably go for the 3 years based on this being adenomatous

	High risk – 3 yearly surveillance		Low risk – 5 yearly surveillance
1.	Adenoma found at 1st screening	1.	Hyperplastic polyps & no adenomas
2.	IGF -1 levels elevated	2.	IGF-1 levels normal

Reference

- Jenkins, P.J. and Fairclough, P.D., (2002). Screening guidelines for colorectal cancer and polyps in patients with acromegaly. Gut, 51(suppl 5), pp.v13-v14.

Question 53

A 52-year-old female has a MRI scan performed for a mild hyperprolactinaemia (600 mu/l (50-400)). The patient is otherwise well and was referred to endocrinology by the GP who picked up the prolactin whilst requesting bloods for menopausal symptoms. Indeed, the other results show elevated LH/FSH and low oestradiol.

The MRI of the pituitary is reported as normal but, in the report, the radiologist notes a pineal cyst of 0.9cm.

Which of the following is the most appropriate approach to the management of this patient?

- **A)** Arrange repeat scan in 1 year
- **B)** Discuss at the pituitary MDT
- **C)** Reassure and discharge patient
- **D)** Refer for neurosurgical opinion
- **E)** Refer to oncology

Answer

Correct answer : Arrange repeat scan in 1 year

Explanation:

Pineal cysts reported on MRI occurs relatively commonly in around 1-4% of scans. In this case of a pineal cyst, the lesion is highly likely to be benign. The lesion should be reviewed with a repeat scan in one year to ensure that there are no size changes.

Reference:

- Pineal cysts and other pineal region malignancies: determining factors predictive of hydrocephalus and malignancy. Robert M. Starke MD, MSc 1 , Justin M. Cappuzzo MD 2 , Nicholas J. Erickson BS 2 and Jonathan H. Sherman MD 3.

Question 54

A 72-year-old man attends clinic complaining of hypersexuality over the last 3-4 months. He has been aware of problems associated with desire and libido which are entirely out of context with his usual status. He finds images in the press sexually stimulating and feels a desire to masturbate frequently. His wife is very concerned as he has not been like this ever before and this behaviour is damaging their relationship of 40 years. He admits to having made sexual advances to female friends too.

One year ago, he was diagnosed with a prolactinoma associated with partial hypopituitarism, for which he has been treated with cabergoline (0.5mg daily) and thyroxine (100mcg daily). He did not want to be treated with testosterone, although his testosterone was 7.2 nmol/l (8-30) with normal LH and FSH concentrations. He also takes sertraline for anxiety at a dose of 100mg daily, atorvastatin 40mg daily, metformin and dapagliflozin with a recent diagnosis of type 2 diabetes.

The prolactin concentration has fallen from 22,000 mu/l to 750 mu/l (<400). A repeat MRI reveals considerable shrinkage of the prolactinoma which expands the sella, extends to both cavernous sinuses and into the suprasellar space but does not impinge on the chiasm. His testosterone is now 15.1 nmol/l.

Which of the following is the most appropriate approach to the management of this patient?

- **A)** Commence cyproterone acetate
- **B)** Commence finasteride
- **C)** Commence LHRH analogue
- **D)** Stop the cabergoline
- **E)** Stop the dapagliflozin

Answer

Correct answer : Stop the cabergoline

Explanation:

Dopamine agonists in the treatment of prolactinomas can be associated with impulse control disorders in up to 10% of treated patients if one looks closely enough. The commonest symptom is hypersexuality (described by some as Dopa-Testotoxicosis) but other features include gambling and impulsive spending. In this patient, with the adverse effects being so profound, cabergoline should be stopped. Consideration can be given to trying an alternative DA such as quinagolide or re-starting at a lower dose, although in this case, the dose is quite low. In this case, the lesion is not sight-threatening, so observation could be an approach in the absence of DA therapy. However, surgery may be required just as in subjects intolerant of DAs.

Reference:

- Bancos, I., Nippoldt, T.B. and Erickson, D., 2017. Hypersexuality in men with prolactinomas treated with dopamine agonists.

Question 55

A 72-year-old man attends clinic complaining of hypersexuality over the last 3-4 months. He has been aware of problems associated with desire and libido which are entirely out of context with his usual status. He finds images in the press sexually stimulating and feels a desire to masturbate frequently. His wife is very concerned as he has not been like this ever before and this behaviour is damaging their relationship of 40 years. He admits to having made sexual advances to female friends too.

One year ago, he was diagnosed with a prolactinoma associated with partial hypopituitarism, for which he has been treated with cabergoline (0.5mg daily) and thyroxine (100mcg daily). He did not want to be treated with testosterone, although his testosterone was 7.2 nmol/l (8-30) with normal LH and FSH concentrations. He also takes sertraline for anxiety at a dose of 100mg daily, atorvastatin 40mg daily, metformin and dapagliflozin with a recent diagnosis of type 2 diabetes.

The prolactin concentration has fallen from 22,000 mu/l to 750 mu/l (<400). A repeat MRI reveals considerable shrinkage of the prolactinoma which expands the sella, extends to both cavernous sinuses and into the suprasellar space but does not impinge on the chiasm. His testosterone is now 15.1 nmol/l.

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Question 1

A 22 year old law student is referred to clinic with a 2 month history of progressive polydipsia and polyuria and also complains of unplanned weight loss in the region of 5 kg over the last 3 months. She has a 25 year old sister diagnosed with type 1 diabetes 5 years previously. On examination her BMI is 20 kg / m^2 her body weight is 64 kg, her blood pressure is 112 / 66 mmHg and visual acuity 6/ 9 in both eyes.
Investigations reveal:

Fasting plasma glucose	14.9 mmol/l	(3.5 - 5.6)
Hba1c	119.7 mmol/mol (13.1%)	(<42.1 mmol/mol (6))
T4	13.9 pmol/l	(9.3 - 23.4)
TSH	0.51 mu/l	(0.32 - 5)

Which of the following is a recognized feature of type 1 diabetes?

- **A)** Association with a single susceptibility locus
- **B)** HLA genes on chromosome 6 are closely linked to immune modulation
- **C)** High prevalence in Asia
- **D)** More Islet cell destruction in late onset type 1 diabetes compared with classical type1 diabetes.
- **E)** Malnutrition in utero may be linked with increased risk of developing Type 1 diabetes

Answer

Correct answer : HLA genes on chromosome 6 are closely linked to immune modulation HLA DR3 / DR4 on chromosome 6 are common genetic markers for type 1 diabetes. Diabetes associated with polyglandular endocrinopathy (Schmidt syndrome) preferentially occurs in middle age women and is strongly associated with HLA-DR-3. Type 1 diabetes has a higher prevalence in northern European and Scandinavian countries and relatively low prevalence in Asia. The histological features of islets from patients with late onset type 1 diabetes are similar to those from patients with classical type 1 diabetes, although there may be differences in major histocompatibility complex expression, with fewer islets being affected in late onset compared with classical type 1 diabetes.

Question 2

A 27 year old man is referred to the lipid clinic following a routine lipid blood test at his surgery which revealed turbid looking plasma with a total cholesterol measuring 6.9 mmol/l (< 4) and plasma triglyceride measuring 10.9 mmol/l (<1.7).

Which of the following would indicate a diagnosis of type III hyperlipoproteinaemia for this patient?

- **A)** Apo E2 / E2 genotype with increased LDL and chylomicron concentrations.
- **B)** Apo E2 / E4 genotype with increased LDL and chylomicron concentrations.
- **C)** Apo E4 / E4 genotype with increased LDL and chylomicron concentrations.
- **D)** Apo E2 / E2 genotype synthesis with increased IDL and chylomicron concentrations.
- **E)** Apo E 4/ E4 genotype with increased VLDL and chylomicron synthesis.

Answer

Correct answer : Apo E2 / E2 genotype synthesis with increased IDL and chylomicron concentrations.

Type III hyperlipoproteinaemia occurs as a consequence of elevated chylomicron and IDL (intermediate density lipoprotein) concentrations. Also known as broad beta disease or dysbetalipoproteinaemia, the most common cause for this form is the presence of Apo E2/E2 genotype. It is due to cholesterol-rich VLDL (β-VLDL). Prevalence is 0.02% of the population. Apolipoprotein E (APOE) is an apoprotein found in chylomicron and IDL particles that binds to a specific receptor on liver cells and peripheral cells. It is essential for the normal catabolism of triglyceride-rich lipoprotein constituents. APOE was initially recognized for its importance in lipoprotein metabolism and cardiovascular disease. More recently, it has been studied for its role in several biological processes not directly related to lipoprotein transport, including Alzheimer's disease, immuno-regulation, and cognition. Defects in APOE result in familial dysbetalipoproteinaemia, or type III hyperlipoproteinaemia (HLP III), in which increased plasma cholesterol and triglycerides are the consequence of impaired clearance of chylomicron, VLDL and LDL remnants.

APOE is 299 amino acids long and transports lipoproteins, fat-soluble vitamins, and cholesterol into the lymph system and then into the blood. It is synthesized principally in the liver, but has also been found in other tissues such as the brain, kidneys, and spleen. In the nervous system, non-neuronal cell types, most notably astroglia and microglia, are the primary producers of APOE, while neurons preferentially express the receptors for APOE. There are seven currently identified mammalian receptors for APOE which belong to the evolutionarily conserved low density lipoprotein receptor gene family.

Question 3

A 26 year old lady is referred to the lipid clinic for assessment. She is well and is currently taking no medication. She was referred by her GP following having her lipid profile measured prior to commencing the oral contraceptive pill. She has a strong family history of cardiovascular disease with her mother suffering a myocardial infarction at the age of 54. On examination her blood pressure is 134 / 75 mmHg, her BMI is 27 kg / m^2 and no definitive tendon xanthomata can be seen.
Investigations reveal:

		Normal Ranges
Turbid Plasma		
Total Cholesterol	7.1 mmol/l	(<5)
Plasma Triglyceride	8.9 mmol/l	(0.9 - 2.2)
Apo E2 / E2 Genotype	Positive	
TSH	2.1 mu / l	(0.32 - 5.5)

What would be the drug of choice to treat this patient's dyslipidemia

- **A)** Atorvastatin
- **B)** Ezetimibe
- **C)** Fenofibrate
- **D)** Nicotinic acid
- **E)** Omega - 3 fish oil

Answer

Correct answer : Fenofibrate

This lady has type III familial hyperlipoproteinaemia based on the detection of an APO E2 genotype. Type III hyperlipoproteinaemia occurs as a consequence of high chylomicrons and IDL (intermediate density lipoprotein). Also known as broad beta disease or dysbetalipoproteinaemia, the most common cause for this form is the presence of Apo E2/E2 genotype. It is due to cholesterol-rich VLDL (β-VLDL). Prevalence is 0.02% of the population, a fibrate is the agent of choice for the management of this form of dyslipidaemia

Question 4

A 31 year old man is referred to the lipid clinic for assessment following a lipid profile carried out by his GP as part of a routine employment medical. On examination his blood pressure is 125/75 mmHg, his BMI is 28 kg/m^2 and no obvious tendon xanthomata can be identified. On questioning he is currently taking no medication, has no family history of note and drinks alcohol infrequently.
Investigations reveal:

		Normal Ranges
Fasting plasma glucose	6.8 mmol/l	(3.5- 5.6)
Total cholesterol	8.1 mmol/l	(< 5)
Plasma Triglyceride	9.5 mmol/l	(0.9 - 2.2)
TSH	2.1 mu / l	(0.32 - 5.5)
AST	89 iu / l	(5 - 45)
ALP	112 iu / l	(30 - 115)
Gamma GT	96 iu / l	(8 - 70)
Hb	13.9 g /dl	(12-16)
MCV	84 fl	(80 - 98)
Uric acid	8.8 mg/ dl	(3.5 - 8.5)
Plasma electrophoresis	Increased VLDL and chylomicron concentrations	

Which of the following is the correct diagnosis for this patient?

- **A)** Primary hyperlipoproteinaemia
- **B)** Type III familial hyperlipoproteinaemia
- **C)** Type V hyperlipoproteinaemia
- **D)** Type IIb combined hyperlipidaemia
- **E)** Type IV hyperlipoproteinaemia

Answer

Correct answer : Type V hyperlipoproteinaemia

Type V hyperlipoproteinaemia or endogenous hypertriglyceridaemia is characterized by an excess of VLDL and chylomicron particles and reduced LPL activity along with elevated hepatic transaminases. The serum has a creamy top layer and turbid bottom. Treatment is either with a fibrate or nicotinic acid. Type V hyperlipoproteinaemia is also associated with glucose intolerance and hyperuricemia.

Question 5

A 32 year old man is referred to the lipid clinic following a routine fasting lipid profile carried out by his GP which reveals a total cholesterol level of 8.3 mmol/l (<4) and a plasma triglyceride level of 18.6 mmol/l (<1.7). He has no family history of note, denies any alcohol excess and other investigations include a fasting plasma glucose of 5.3 mmol/l (<5.6), normal thyroid function tests, liver function tests and renal function. On examination his blood pressure is 135 / 75 mmHg, his BMI is 27 kg/m^2 and no tendon xanthomata can be found.
Which of the following is a feature of this dyslipidaemia?

- **A)** ApoE dysfunction
- **B)** Lysosomal esterase deficiency
- **C)** LCAT deficiency
- **D)** Reduced lipoprotein lipase activity
- **E)** Reduced hepatic lipase

Answer

Correct answer : Reduced lipoprotein lipase activity

This very rare form (also known as Buerger-Gruetz syndrome, primary hyperlipoproteinaemia, or familial hyperchylomicronemia) is due to a deficiency of lipoprotein lipase (LPL) or altered apolipoprotein C2, resulting in elevated chylomicrons, the particles that transfer fatty acids from the digestive tract to the liver. Lipoprotein lipase is also responsible for the initial breakdown of endogenously made triacylglycerides in the form of very low density lipoprotein (VLDL). As such, one would expect a defect in LPL to also result in elevated VLDL. Its prevalence is 0.1% of the population.

Apolipoprotein C2 is an apolipoprotein responsible for the activation of lipoprotein lipase (LPL) in capillaries and thus begins the catabolism of the chylomicrons and VLDL. It is also found in HDL. Deficits of this apoprotein C2 present with grave hypertriglyceridemia and hyperchylomicronemia during fasting

Question 6

A 48 year old lady is referred to the lipid clinic following a fasting lipid profile checked by her GP. She has no family history or past medical history of note. She is a non-smoker, is receiving no regular medication and drinks alcohol infrequently. On examination her blood pressure is 160 / 85 mmHg, her BMI is 33 kg / m^2 her waist circumference is 92 cm and she has no evidence of tendon xanthomata.
Investigations reveal:

		Normal Ranges
Fasting Plasma Glucose	6.8 mmol/l	(3.5 - 5.6)
Total Cholesterol	6.9 mmol/l	(<5)
Plasma Triglyceride	5.1 mmol/l	(0.9 - 2.2)

Which of the following is a feature of type IIb combined hyperlipidaemia?

- **A)** Characterized by elevated IDL and VLDL concentrations
- **B)** Characterized by elevated VLDL and chylomicron concentrations
- **C)** Characterized by elevated LDL and VLDL concentrations
- **D)** Prevalence in the population is around 30%
- **E)** Results from reduced LPL activity and APO A1 concentrations

Answer

Correct answer : Characterized by elevated LDL and VLDL concentrations

Type IIb hyperlipidaemia is characterized by elevated concentrations of Apo B containing particles in particular LDL and VLDL. The high VLDL levels are due to overproduction of substrates, including triglycerides, acetyl CoA, and an increase in B-100 synthesis. They may also be caused by the decreased clearance of LDL. Prevalence in the population is 10%. Type IIb hyperlipidaemia may arise in the context of either familial combined hyperlipoproteinaemia (FCH) or secondary combined hyperlipoproteinaemia resulting from the metabolic syndrome (for which it forms part of the diagnostic criteria) or type 2 diabetes.

Question 7

A 41 year old man is referred to the lipid clinic following a routine fasting lipid sample collected by his GP. He has no past medical history of note, is a non-smoker and denies any excess alcohol consumption. On examination his blood pressure is 145 / 75 mmHg, his BMI is 29 kg / m^2 his waist circumference is 88 cm and no tendon xanthoma can be identified.
Investigations reveal:

		Normal Ranges
Fasting Plasma Glucose	5.4 mmol/l	(3.5 - 5.6)
Total Cholesterol	6.1 mmol/l	(<5)
Plasma triglyceride	9.9 mmol/l	(0.9 - 2.2)

Which of the following is a feature of type IV familial hyperlipemia?

- **A)** Characterized by increased chylomicron concentrations
- **B)** Characterized by increased VLDL concentrations
- **C)** Has a population prevalence of around 30%
- **D)** Results from defective lipoprotein lipase activity
- **E)** Statins are the mainstay of treatment

Answer

Correct answer : Characterized by increased VLDL concentrations

Type IV hyperlipoproteinaemia also known as hypertriglyceridaemia has a population prevalence according to NCEP APT III classification of hypertriglyceridaemia of around 16%. It is characterized by increased levels of VLDL as a result of increased synthesis and reduced clearance. One of the major clinical consequences of hypertriglyceridaemia is an increased risk of pancreatitis and fibrates are the mainstay of therapy.

Question 8

A 35 year old lady is referred to the lipid clinic following the measurement of her fasting lipid profile by her GP. She is a non smoker and drinks alcohol very infrequently and exercises regularly. She has a strong family history of cardiovascular disease with her older brother requiring coronary bypass surgery at the age of 41 and her mother suffering an MI at the age of 47. On examination her blood pressure is 133 / 61 mmHg and her BMI is 24 kg / m^2
Investigations reveal:

		Normal Ranges
Total Cholesterol	7.6 mmol/l	(<5)
LDL-Cholesterol	5.9 mmol/l	(<2)
Plasma Triglyceride	1.1 mmol/l	(0.9 - 2.2)
HDL-Cholesterol	1.2 mmol/l	(>1.2)

Which of the following is a feature of familial hypercholesterolemia (FH)?

- **A)** Arises from mutations of the LDL-receptor on the short arm of chromosome 16
- **B)** Diagnosis is based on LDL and total cholesterol levels above the 75th centile combined with appropriate family history, tendon xanthomata and xanthelasma
- **C)** Heterozygous FH has a population prevalence of 1:5000 in most countries
- **D)** LDL receptor mutations account for 90% of cases of FH.
- **E)** Thickening of the Achilles tendon is a characteristic physical sign associated with FH

Answer

Correct answer : Thickening of the Achilles tendon is a characteristic physical sign associated with FH

Familial hypercholesterolemia (FH) is characterized by raised serum LDL cholesterol levels, which result in excess deposition of cholesterol in tissues, leading to accelerated atherosclerosis and increased risk of premature coronary heart disease. In most populations studied, heterozygous FH occurs in about 1:500 people, but not all develop symptoms. Homozygous FH occurs in about 1:1,000,000. FH results from defects in the hepatic uptake and degradation of LDL via the LDL-receptor pathway, commonly caused by a loss-of-function mutation in the LDL-receptor gene (LDLR) on the short arm of chromosome 19 or by a mutation in the gene encoding apolipoprotein B (APOB). FH is primarily an autosomal dominant disorder with a gene-dosage effect. An autosomal recessive form of FH caused by loss-of-function mutations in LDLRAP1, which encodes a protein required for clathrin-mediated internalization of the LDL receptor by liver cells, has also been documented. LDLR mutations are more common in certain populations, presumably because of a genetic phenomenon known as the founder effect—they were founded by a small group of individuals, one or several of whom was a carrier of the mutation. The Afrikaner, French Canadians, Lebanese Christians, and Finns have high rates of specific mutations that make FH particularly common in these groups. APOB mutations are more common in Central Europe.

The most recent addition to the database of genes in which defects cause FH is one encoding a member of the proprotein convertase family, PCSK9. Rare dominant gain-of-function mutations in PCSK9 cosegregate with hypercholesterolemia, and one mutation is associated with a particularly severe FH phenotype. Expression of PCSK9 normally down-regulates the LDL-receptor pathway by indirectly causing degradation of LDL-receptor protein, and loss-of-function mutations in PCSK9 result in low plasma LDL levels.

The diagnosis of FH is primarily based on clinical grounds and may be confirmed by genetic testing. Typical clinical features include cholesterol deposition in the tendons resulting in the formation of tendon xanthomata, with thickening of the Achilles tendon being an early classical coetaneous manifestation of FH. Such soft tissue manifestations combined with LDL-cholesterol levels above the 95th centile and a family history of premature cardiovascular disease which classically demonstrates intra-familial concordance of onset suggests a diagnosis of FH. Subsequent genetic testing for LDL-receptor and Apo B mutations reveal mutations in between 50 and 80% of cases; those without a mutation often have higher triglyceride levels and may in fact have other causes for their high cholesterol, such as

combined hyperlipidaemia due to metabolic syndrome.

FH is usually treated with statins. Statins act by inhibiting the enzyme hydroxymethylglutaryl CoA reductase (HMG-CoA-reductase) in the liver. In response, the liver produces more LDL receptors, which remove circulating LDL . Statins effectively lower cholesterol and LDL levels, although sometimes add-on therapy with other drugs is required, such as bile acid sequestrants (cholestyramine or colestipol), nicotinic acid preparations or fibrates. Control of other risk factors for cardiovascular disease is required, as risk remains somewhat elevated even when cholesterol levels are controlled. Professional guidelines recommend that the decision to treat an FH patient with statins should not be based on the usual risk prediction tools (such as those derived from the Framingham Heart Study), as they are likely to underestimate the risk of cardiovascular disease; unlike the rest of the population, FH have had high levels of cholesterol since birth, probably increasing their relative risk. The addition of ezetimibe may also be a therapeutic option. Although controversy persists around the role of ezetimibe due to the absence of a significant effect of combination ezetmibe / statin compared with statin monotherapy on carotid intima-media thickness in patients with FH.

There are no interventional studies that directly show mortality benefit of cholesterol lowering in FH patients. Rather, evidence of benefit is derived from a number of trials conducted in people who have polygenic hypercholesterolemia (in which heredity plays a smaller role). Still, an observational study of a large British registry showed that mortality in FH patients had started to improve in the early 1990s, when statins were introduced.

Homozygous FH is harder to treat. The LDL receptors are minimally functional, if at all. Only high doses of statins, often in combination with other medications, are modestly effective in improving lipid levels. If medical therapy is not successful at reducing cholesterol levels, LDL apheresis may be used; this filters LDL from the plasma in a process reminiscent of dialysis. Very severe cases may be considered for a liver transplant leading to rapid improvement in cholesterol levels, but at the risk of complications from any solid organ transplant. Other surgical techniques include partial ileal bypass surgery, in which part of the small bowel is bypassed to decrease the absorption of cholesterol, and portacaval shunt surgery, in which the portal vein is connected to the vena cava thus by-passing liver metabolism. Inhibition of the microsomal triglyceride transfer protein, for example with the investigational drug AEGR-733, and infusion of recombinant human apolipoprotein A1 are being explored as medical treatment options, with gene therapy also as a possible future alternative.

Given that FH is present from birth and atherosclerotic changes may begin early in life, it is sometimes necessary to treat adolescents or even teenagers with agents that were originally developed for adults. Due to safety concerns, many doctors prefer to use bile acid

sequestrants and fenofibrate as these are licensed in children. Nevertheless, statins seem safe and effective, and in older children may be used as in adults.

A multidisciplinary expert panel in 2006 advised on early combination therapy with LDL apheresis, statins and cholesterol absorption inhibitors in children with homozygous FH at the highest risk.

Question 9

A 45 year old Asian man is reviewed by his GP as part of a cardiovascular risk factor screening programme. He is a non-smoker with the only family history of note being his father who has been diagnosed with type 2 diabetes at the age of 68 following admission to hospital with an episode of troponin-negative chest pain. On examination his blood pressure is 165 / 75 mmHg, his BMI is 28 kg / m^2 and his waist circumference is 89 cm
Investigations reveal:

		Normal Ranges
Fasting Plasma Glucose	5.5 mmol/l	(3.5 - 5.6)
Fasting Total Cholesterol	5.6 mmol/l	(<5)
Fasting Plasma Triglyceride	1.7 mmol/l	(0.9 - 2.2)
HDL-Cholesterol	0.8 mmol/l	(0.9 - 1.8)
LDL-Cholesterol	3.8 mol/l	(< 3)
TSH	2.1 mu/l	(0.32 - 5.5)

How would you manage this gentleman’s lipid profile?

- **A)** Atorvastatin 20 mg OD
- **B)** Diet / lifestyle modification
- **C)** Rosuvastatin 10 mg OD
- **D)** Omega fatty acids
- **E)** Ezetimibe 10mg OD

Answer

Correct answer : Diet / lifestyle modification

Estimate the level of risk using the QRISK2 assessment tool. The 10 year cardiovascular risk in this gentleman is less than 10% according to QRISK2 Score - in fact this is 9.6% based on a BMI of 28. Therefore, the most appropriate advice here would be for lifestyle changes initially and probable antihypertensive treatment.

Question 10

A 46 year old man undergoes cardiovascular risk factor screening by his GP as part of a routine life insurance medical. On examination his BMI is 31 kg / m^2 and his blood pressure is 155 / 85 mmHg.
Investigations reveal:

		Normal Ranges
Fasting Plasma Glucose	5.5 mmol/l	(3.5 - 5.6)
Fasting Cholesterol	5.3 mmol/l	(<5)
HDL-Cholesterol	0.9 mmol/l	(0.8 - 1.9)
LDL-Cholesterol	2.9 mmol/l	(< 3)
Fasting Plasma triglyceride	1.6 mmol/l	(0.9 - 2.2)

When initially assessing a patient's risk of cardiovascular disease which of the following lipid profiles is most important?

- **A)** Random total cholesterol level
- **B)** Fasting Total cholesterol and HDL-C levels
- **C)** Fasting Total cholesterol and plasma Triglyceride levels
- **D)** Fasting Total and LDL-Cholesterol levels
- **E)** Fasting LDL and HDL-cholesterol levels

Answer

Correct answer : Fasting Total cholesterol and HDL-C levels

NICE guidelines now state that a person's 10 year CVD risk should be assessed using a QRISK2 assessment calculator and based on TC:HDL ratio. Other factors used in this calculation include, age, gender, smoking status, blood pressure and presence or otherwise of LVH. The role of including diabetes status in this calculation remains debatable as the source data for this calculator (Framingham risk equation) underestimates CVD risk associated with diabetes, with diabetes increasing the risk of CVD by 2- 3 times that of the non-diabetic population. Family history and ethnicity are also important factors with premature family history requiring a multiplication factor of 2 and Asian ethnicity a factor of 1.4 to be applied to the initial CVD risk calculation.

Question 11

A 45 year old female is receiving orlistat 120 mg tds for assistance with weight loss. Prior to commencing orlistat, the patient's weight was 108 kg and her BMI was 36.8 kg/m^2. The patient re-attends clinic, three months after commencing orlistat and her weight is now 102.2kg. She is keen to continue orlistat as she feels it has helped her and has only been aware of occasional diarrhoea. Which of the following is the most appropriate approach to her management?

- **A)** Add topiramate 25 mg daily
- **B)** Continue orlistat at current dose
- **C)** Increase dose of orlistat to 150 mg tds
- **D)** Reduce dose of orlistat to 60 mg tds
- **E)** Stop Orlistat

Answer

Correct answer : Continue orlistat at current dose

This patient has lost 5.8 kg of weight over three months equating to roughly a 5% weight loss which is the figure recommended by NICE CG 189supporting continued treatment. The maximal orlistat dose is 120mg tds and there is no value in increasing this.

Question 12

A 50-year-old female is referred with a 3-month history of tiredness and fatigue. Her GP had checked some bloods and found that she was euthyroid but had a triglyceride of 11.1 mmol/l (<2.5), a cholesterol of 7 mmol/l (3.5-5.5) and glucose of 5.3 mmol/l. She has a 12-month history of breast cancer Stage 1 for which she takes tamoxifen 20mg/d, and also anxiety for which she takes sertraline 100mg daily, GORD for which she takes omeprazole 20 mg daily, and hay fever for which she takes occasional chlorpheniramine.

She has a strong family history of coronary artery disease with her father having died of a MI at 45, although he was a smoker and her paternal uncle having had coronary artery bypass before the age of 50.

On examination, she has a BMI of 29kg/m^2, appears clinically euthyroid, and there are no xanthomas/xanthelasma. Blood pressure was 122/80mmhg and nothing else was to be found on examination.

Fasting bloods revealed:

Test	Result	Normal Range
Triglycerides	6.5 mmol/l	
Cholesterol	7.1 mmol/l	
Glucose	4.2 mmol/l	
LFTs	Normal	
T4	9.3 nmol/l	(9-21)
TSH	2.1 mu/l	(0.5-4.5)

Which of the following is the likely cause for her hypertriglyceridaemia?

- **A)** Chlorpheniramine
- **B)** Familial combined hyperlipidaemia
- **C)** Secondary hypothyroidism
- **D)** Sertraline
- **E)** Tamoxifen

Answer

Correct answer : Tamoxifen

Explanation:

This patient has marked hypertriglyceridaemia as well as associated hypercholesterolaemia. There are a number of causes of the former including drugs such as thiazides, steroids and oestrogens. Tamoxifen which is a SERM has oestrogen-like activity, and hypertriglyceridaemia is reported as a side effect to such severity that it has also been reported in conjunction with pancreatitis. In this case, its continued use could be discussed with an oncologist to assess if an alternative might be appropriate such as letrozole.

This patient's family history is more in keeping with familial hypercholesterolaemia than combined hyperlipidaemia as her paternal side of the family presents with premature coronary artery disease.

Reference:

- Singh, H.K., Prasad, M.S., Kandasamy, A.K. and Dharanipragada, K., 2016. Tamoxifen-induced hypertriglyceridemia causing acute pancreatitis. Journal of pharmacology & pharmacotherapeutics, 7(1), p.38.

Question 13

A 42 year old female is commenced on orlistat as treatment of her obesity. Through which of the following mechanisms does orlistat function in helping to reduce weight?

- **A)** Combined noradrenergic/serotonergic uptake inhibitor
- **B)** Endocannabinoid receptor antagonist
- **C)** GLP-1 receptor agonist
- **D)** Intestinal lipase inhibitor
- **E)** PYY 3-36 agonist

Answer

Correct answer : Intestinal lipase inhibitor

Orlistat is an effective agent to assist with weight loss acting as a lipase inhibitor reducing the absorption of fat from the GI tract by the order of approximately 30%. Thus, side effects of orlistat include flatulence, watery diarrhoea and GI upset.

Question 14

A 50 year old male seeks advice regarding treatment of his obesity. He has had a struggle with weight problems for many years and has had difficulty losing weight with diet and exercise regimes. He has not tried any medical therapies.

On examination, his weight is 142 kg and his BMI is 51 kg/m^2. His blood pressure is 136/84 mmHg and his pulse is 72 bpm.

Investigations reveal:

U+Es	Normal
Fasting Glucose	8.2 mmol/l

Which of the following would be the most appropriate approach to his weight management?

- **A)** Recommend admission for supervised very low calorie diet (600 kcal/d)
- **B)** Recommend for bariatric surgery
- **C)** Recommend metformin
- **D)** Recommend orlistat 60 mg tds
- **E)** Recommend orlistat 120 mg tds

Answer

Correct answer : Recommend for bariatric surgery

The most appropriate treatment for this patient's weight problems is bariatric surgery. NICE recommend bariatric surgery as the primary treatment modality in individuals with a BMI above 50. In this patient, the fasting plasma glucose also suggests a diagnosis of diabetes, yet the question focuses on weight management and so metformin is really not associated with any real weight loss. Again, the very low calorie diets have little to support their use for sustained weight loss.

Question 15

A 28 year old female has been struggling with her weight for a number of years and now attends clinic. She has tried a number of dietary schemes without much success and is currently trying to employ a hypocaloric diet. She has a history of polycystic ovarian syndrome and has been advised from the gynaecological clinic that she needs to lose weight. Lately she has also been a little tearful concerning her weight and is occasionally tearful during the consultation. Currently she is not taking any treatment. Her weight is 86 kg and she has a BMI of 27.8 kg/m^2. Her pulse is 72 bpm and her blood pressure is 126/78 mmHg. She is keen to receive some kind of intervention to help with her weight loss. Which of the following would you recommend?

- **A)** Bariatric surgery
- **B)** Continue with education, diet and exercise
- **C)** Fluoxetine
- **D)** Orlistat
- **E)** Topiramate

Answer

Correct answer : Continue with education, diet and exercise

This young female has a BMI indicating that she is overweight. The NICE criteria recommends pharmacological intervention in patients with a BMI above 28 with co-morbidities (like type 2 diabetes, hypertension, cardiovascular disease, osteoarthritis, dyslipidaemia and sleep apnoea) or a BMI >30 without co-morbidities. The presence of PCOs does not fulfill this criteria and the patient should be counselled and advised on adhering to a hypocaloric diet which should be complemented by an appropriate exercise regime.

Question 16

A 16 year old male with severe obesity is diagnosed with Laurence-Moon-Biedl syndrome. Which of the following is the mode of inheritance of this condition?

- **A)** Autosomal dominant
- **B)** Autosomal recessive
- **C)** Mitochondrial
- **D)** X-linked dominant
- **E)** X-linked recessive

Answer

Correct answer : Autosomal recessive

Laurence-Moon-Biedl syndrome is an autosomal recessive disorder that is typified by severe obesity, hypogonadism, hyperphagia and optic atrophy.

Question 17

A 44 year old female attends the weight management service. She has a three year history of diet controlled type 2 diabetes with a HbA1c of 49.7 mmol/mol (6.7%). She has been unsuccessful in losing weight over the last 1 year. Most recently she is taking orlistat 200 mg tds for the last three months and her weight has fallen by 1 kg. Her BMI is 38.8 kg/m^2. She remains frustrated at not being able to lose weight and is keen to receive treatment.
Which of the following would you recommend?

- **A)** Add metformin to current dose of orlistat
- **B)** Continue with orlistat for further 3 months
- **C)** Increase dose of orlistat
- **D)** Stop orlistat and refer for bariatric surgery
- **E)** Stop orlistat and refer for further dietary advice

Answer

Correct answer : Stop orlistat and refer for bariatric surgery

This patient has failed to lose appropriate weight using medical therapies. The orlistat should be stopped and the patient does fulfil the criteria for bariatric surgery and this should be considered. Laparoscopic banding is the recommended treatment for patients with a BMI above 35 with an associated co-morbidity (such as diabetes) and for those patients with a BMI above 40. In patients with a BMI above 50, bariatric surgery is regarded as the primary therapeutic modality.

Question 18

A 62 year old male is being treated for ischaemic heart disease with simvastatin. However, he develops myalgia whilst taking this treatment and is switched to ezetimibe.
Which of the following best describe the mechanism of action of ezetimibe?

- **A)** A 3-HMG-CoaA inhibitor
- **B)** PPAR-alpha agonist
- **C)** PPAR-gamma agonist
- **D)** Reduces cholesterol reabsorption through inhibition of cholesterol transport protein
- **E)** Reduces cholesterol reabsorption through binding intestinal bile salts

Answer

Correct answer : Reduces cholesterol reabsorption through inhibition of cholesterol transport protein

Ezetimibe is a new class of cholesterol lowering agent which acts through the inhibition of a cholesterol transport protein reducing the reabsorption of cholesterol from the GI tract. It may therefore contribute to an approximate 20% reduction in total cholesterol concentrations and is a useful agent in those unable to take statins - HMG-CoA inhibitors.

Question 19

A 45 year old male attends the weight management service. He receives advice from the nurse regarding diet and exercise as his BMI is 33 kg/m^2. He is informed about a hypocaloric diet particularly in relation to his total daily energy expenditure and hence the likely weight loss one would see from this calorie restriction. He enquires as to what is his total daily energy expenditure.

Which of the following is the total daily energy expenditure for an average male?

- **A)** 1000 kcal
- **B)** 1500 kcal
- **C)** 2000 kcal
- **D)** 2500 kcal
- **E)** 3000 kcal

Answer

Correct answer : 2500 kcal

The typical total energy expenditure for a male is 2500 kcal/d and 2000 kcal per day for a female. Of course, with increasing weight, the patient will have increased total energy expenditure but these averages are important as restricting calorie intake to recommended levels of 1500-1600 kcals/d will result in a calorie deficit which translates into approximately 0.5 kg weight loss per week.

Question 20

A 21 year old male presents with a long history of weakness, muscle cramps and ease of fatigue. He denied use of any illicit substances and was otherwise fine. His mother had type 2 diabetes and he had two other brothers who were well. There was little of note on examination, his BMI was 29 kg/m^2 and the following results were obtained:

		Normal Ranges			
U+Es	Normal				
AST	94 iu/l	(5 - 40)			
ALT	90 iu/l	(5 - 40)			
Alkaline phosphatase	88 ui/l	(50 - 110)			
Bilirubin	12 micromol/l	(0 - 18)	**CPK**	1020 iu/l	(30 - 220)
LDH	300 iu/l	(90 - 250)			
Calcium	2.4 mmol/l	(2.2 - 2.6)			
Antibody screen	Negative				
FBC	Normal				
ESR	10 mm/hr	(0 - 15)			

Which of the following is the most likely diagnosis?

- **A)** Becker's muscular dystrophy
- **B)** McArdle's disease
- **C)** Non-alcoholic steatohepatosis
- **D)** Thyrotoxic periodic paralysis
- **E)** Vitamin D Deficiency

Answer

Correct answer : McArdle's disease

The most likely diagnosis in this scenario is McArdle's disease, a type V glycogen storage disorder associated with myophosphorylase deficiency resulting in a reduction in the glycogenolysis within muscle. This is not likely to be thyrotoxic periodic paralysis as typically the CPK is normal. Nor is this likely to be Becker’s Muscular dystrophy as weakness is reported without any obvious muscle loss or fasciculation. The so-called ‘liver enzymes’ are also found in muscle and signify damage. Often the CPK may be elevated after doing some exercise.

Question 21

A 44 year old male with a long history of epilepsy and associated learning difficulties was admitted as his carers felt that he was more subdued and unwell. There was little history to obtain directly although his carers stated that he was normally much brighter and communicative. He was taking omeprazole for GORD, thyroxine, olanzapine, co-codamol on a PRN basis, topiramate and had recently been prescribed co-trimoxazole by his GP for assumed UTI.

On examination, he appeared subdued and uncommunicative with a GCS of 15. His temperature was 37.2 °C, blood pressure 118/72 mmHg, pulse of 110 bpm, oxygen saturations of 98% on air and a respiratory rate of 30/min. No specific signs were noted on examination of the chest, praecordium or abdomen. No focal neurology was noted.

Investigations revealed:

		Normal Ranges
FBC	Normal	
Sodium	144 mmol/l	(134 - 144)
Potassium	3.9 mmol/l	(3.5 - 5)
urea	10.2 mmol/l	(3 - 8)
Creatinine	140 micromol/l	(50 - 100)
Chloride	122 mmol/l	(95 - 105)
Fasting Plasma Glucose	7.8 mmol/l	(3.5 - 5.6)
pH	7.12	(7.35 - 7.45)
Standard bicarbonate	11 mmol/l	(22 - 28)
pCO2	4.2 kPa	(4.5 - 6)
pO2	14.5 kPa	(10 - 13)
Lactate	1.2 mmol/l	(0.5 - 1.5)

Which of the following is the likely diagnosis?

- **A)** Co-trimoxazole induced acidosis

- **B)** Diabetic ketoacidosis
- **C)** Methanol consumption
- **D)** Olanzapine induced acidosis
- **E)** Topiramate induced acidosis

Answer

Correct answer : Topiramate induced acidosis

The patient has a hyperchloraemic acidosis with a normal anion gap {sodium – (bicarbonate+chloride) = 11 – NR 8-16}. In this case the normal anion gap would exclude all the typical causes as found with high anion gap – lactic acidosis, DKA, methanol etc (A useful mnemonic for high anion gap metabolic acidosis is MUDPILES). Loss of bicarbonate ions is often a cause of normal anion gap acidosis – renal tubular acidosis. In our case, Topiramate causes a type 2 RTA and loss of bicarbonate ions. Acetazolamide, fistulas, hyperparathyroidism are all capable of producing a normal anion gap acidosis.

Question 22

A 44 year old male presents with a three month history of profuse watery diarrhoea. No specific abnormalities are noted on examination and colonoscopy and stool culture are negative. Investigations reveal the following results:

		Normal Ranges
Polypeptide P	210 pmol/l	(<300)
VIP	350 pmol/l	(<30)
Gastrin	33 pmol/l	(<40)
Glucagon	25 pmol/l	(<50)

Which of the following is the most appropriate investigation?

- **A)** Endoscopic ultrasound
- **B)** MRI abdomen
- **C)** No further investigation required
- **D)** Selective pancreatic sampling
- **E)** Somatostatin scintigraphy

Answer

Correct answer : MRI abdomen

This patient appears to have a VIPoma – Verner-Morrison syndrome. This is due to a pancreatic neuroendocrine tumour in over 90% of cases and is associated with profuse watery diarrhoea and fasting vasoactive intestinal peptide (VIP) concentrations typically 10 times elevated. Imaging the pancreas would be the most appropriate step herewith and would be expected to localize the tumour effectively as they are typically larger than 2cm. MRI would be the sensible first step in the investigation of this patient. Surgical resection is the treatment of choice but somatostatin analogues would be used to control symptoms prior to surgery.
Further reading:Vipoma Medscape

Question 23

A 21 year old female is referred to clinic by her general practitioner who is concerned regarding menstrual irregularity and abnormal investigations. She describes rather irregular periods with cycles of between 28-40 days. Her last period was 40 days ago. Her menarche was at the age of 13 and her periods were generally regular. She commenced the oral contraceptive microgynon one year ago for contraception and claims to regularly take this. She denies any use of illicit substances.

She is otherwise well, has a BMI of 30.2 kg/m^2 and has a no abnormalities on examination. The investigations included by the GP reveal:

		Normal Ranges
Thyroid function tests	Normal	
Prolactin	350 mu/l	(<450)
Estradiol	<80 pmol/l	(130-800)
LH	1.2 mu/l	(2-10)
FSH	1.4 mu/l	(2-10)

Which of the following is the likely explanation?

- **A)** Craniopharyngioma
- **B)** Drug induced
- **C)** Non-functioning pituitary tumour
- **D)** Primary ovarian failure
- **E)** Silent pituitary infarction

Answer

Correct answer : Drug induced

This patient has low LH/FSH and undetectable estradiol – a consequence of the use of the combined oral contraceptive – microgynon. The synthetic estrogen, ethinyl estradiol, is used in the OCP and is not detected by 17beta oestradiol assays. Thus, the high concentration of ethinyl oestradiol effectively suppresses LH/FSH and prevents ovulation – this is how it works as an OCP.

This is quite a common referral from general practice. Do not measure estradiol concentrations in patients on the OCP.

Question 24

A 44 year old male presents with a rash in the groin, weight loss and diarrhoea. He is diagnosed with a glucagonoma. Which of the following is the correct diagnosis of this rash?

- **A)** Acrodermatitis enteropathica
- **B)** Epidermolysis bullosa
- **C)** Necrolytic migratory erythema
- **D)** Pellagra
- **E)** Pyoderma gangrenosum

Answer

Correct answer : Necrolytic migratory erythema

The typical rash associated with glucagonoma is a necrolytic migratory erythema which is often located in the perineal region. The underlying histology is inflammation and separation of the superficial layers of the epidermis.

Necrolytic Migratory Erythema

Question 25

A 55 year old female is diagnosed with carcinoid syndrome after presentation with diarrhoea. She is treated with octreotide 50 micrograms tds and is noted to have a marked improvement in her diarrhoea. She is converted to long ating octreotide 30mg monthly but begins to notice that the stools have become rather bulky, pale and oily.

Which of the following is the most likely explanation for this?

- **A)** Diverticular disease
- **B)** Extensive terminal ileal disease
- **C)** Gallstones
- **D)** Pancreatic exocrine deficiency
- **E)** Pancreatic tumour infiltration

Answer

Correct answer : Pancreatic exocrine deficiency

The most likely explanation is pancreatic exocrine insufficiency, a side effect of the octreotide therapy and caused by inhibition of pancreatic enzyme secretion. This is well described and may be treated with pancreatic enzyme supplementation such as creon.

Question 26

You are asked to review a patient on the neurosurgical ward. He has had an aneurysm clipped following subarachnoid haemorrhage but the neurosurgeons are concerned that his sodium concentration has fallen. Currently his sodium concentration is 118 mmol/l. Further investigations reveal:

		Normal Ranges
Urea	4 mmol/l	(3-8)
Potassium	4.4 mmol/l	(3.5-5)
Plasma Osmolality	254 mosmol/l	(275-295)
Urine Sodium	50 mmol/l	
Urine Osmolality	440 mosmol/l	

Which of the following is the most likely explanation of this patient's hyponatraemia?

- **A)** Acute hypoadrenalism
- **B)** Hypovolaemic hyponatraemia
- **C)** Pituitary apoplexy
- **D)** Pseudohyponatraemia
- **E)** Syndrome of inappropriate ADH secretion

Answer

Correct answer : Syndrome of inappropriate ADH secretion

The diagnosis is SIADH, based on the biochemistry results revealing a low sodium, high urine osmolaltiy and the elevated urine sodium (>20). This could be made a very tough question in the exam if you are asked to differentiate between SIADH and cerebral salt wasting. The latter is associated with a typically higher urine sodium (>100) and a evidenced of reduced plasma volume although this is difficult to identify.

Question 27

In a study of 1000 patients, a new serological test for neuroendocrine tumours was assessed against imaging, utilised as the gold standard for the disease. The following results were obtained:

	Test Positive	Test Negative
MRI Positive	80	20
MRI Negative	100	800

To what does the sensitivity of the new test approximate?

- **A)** 50%
- **B)** 60%
- **C)** 70%
- **D)** 80%
- **E)** 90%

Answer

Correct answer : 80%

We are told that the MRI is the gold standard. Therefore, sensitivity of the test is the number of test positives correctly identified (80)/ (number of test positives (80) + false negatives (20)) = 80/100 = 80%. In the case of specificity, this relates to the number of true negatives with the new test (800)/ the number of true negatives (800) + false positives (100). This is approximately 90% (88.9%).

Question 28

A 55 year old male attends for an insurance medical. He is generally fit and has no medical history of note. He is a non smoker and drinks approximately 10 units of alcohol each week. His family history includes his father having died at the age of 54 of a heart attack.

His blood pressure is 132/80 mmHg and his BMI is 31.6 kg/m^2. Blood investigations reveal:

		Normal Ranges
Cholesterol	5.8 mmol/l	(<5)
Triglyceride	1.5 mmol/l	(0.8- 2.0)
HDL	1.0 mmol/l	(0.9 - 1.9)
Plasma Glucose	5.4 mmol/l	(3.5 - 5.6)

He is advised a low cholesterol diet only. By how much would this be expected to lower his cholesterol concentration?

- **A)** 10%
- **B)** 20%
- **C)** 30%
- **D)** 40%
- **E)** 50%

Answer

Correct answer : 10%

This patient has a strong family history of premature cardiovascular disease with his father having died of a MI at the age of 54. In this man's case, risk equations would suggest a 15% risk of a cardiovascular event in the next 10 years which would be regarded as moderate. Yet, when one considers the significant family history, this risk needs to be multiplied by a factor of 1.5, placing him at a high risk in excess of 20%. In this scenario, a healthy diet, low in saturated fats should be suggested. His modest alcohol is protective against cardiovascular disease. Similarly lifestyle interventions such as increased exercise should be encouraged. However, one would wish to target his cholesterol concentration with an aim to reduce his cholesterol to below 5 mmol/l. Diet would be expected to reduce cholesterol by only 10% which would not succeed in achieving target cholesterol. Hence, the most appropriate approach to reducing this patient's cardiovascular risk would be the introduction of a statin which reduces cholesterol by the order of 30-50%.

Reference:

WHO/ISH Risk prediction charts

Question 29

A 71 year old gentleman is admitted to hospital following admission to hospital with a mechanical fall. On admission, his random plasma glucose is 12.4 mmol/l (<7.8) and a subsequent fasting plasma glucose measures 7.9 mmol/l (<6). He is generally well, taking no regular medications and on examination his blood pressure is 146/86 mmHg and his BMI is 31 kg / m^2.

Further investigations reveal:

		Normal Ranges
Hba1c	54.1 mmol/mol (7.1%)	(<42.1 mmol/mol (6))
Total Cholesterol	6.1 mmol/l	(<5)
Plasma Triglyceride	2.1 mmol/l	(0.9 - 2.2)
LDL Cholesterol	3.7 mmol/l	(<2)
HDL Cholesterol	0.9 mmol/l	(0.9 - 1.9)

According to the Strong Heart Study, which of the following is the most important determinant of the future risk of cardiovascular events in this gentleman?

- **A)** Total cholesterol level
- **B)** LDL-cholesterol level
- **C)** HDL-cholesterol level
- **D)** Plasma Triglyceride Level
- **E)** Non-HDL-cholesterol level

Answer

Correct answer : Non-HDL-cholesterol level

The results of the Strong Heart Study indicate that non-HDL-C may be a superior predictor of cardiovascular events than LDL-C; HDL-C or plasma TG levels alone in both men and women with type 2 diabetes. The utility of non-HDL-C in predicting cardiovascular events in non-diabetic subjects is supported by data from the SHEP (Systolic Hypertension in the Elderly Program) and Lipid Research Clinics (LRC) studies, in which non-HDL-C was found to be a better predictor than LDL-C of cardiovascular events in patients followed over 4.5 years and 19 years respectively.

Non-HDL cholesterol includes VLDL, IDL, LPa apart from LDL Cholesterol.

Question 30

A 63 year old female is admitted with a two day history of being unwell and deteriorating confusion. Arterial blood gas analysis reveals:

		Normal Ranges
pH	7.65	(7.36-7.44)
pO2	8 kPa	(11.3-12.6)
pCO2	4.5 kPa	(4.7-6.0)
Standard Bicarbonate	35 mmol/L	(20-28)

Which of the following is the correct interpretation of these blood gas results?

- **A)** Metabolic alkalosis
- **B)** Respiratory alkalosis
- **C)** Laboratory error
- **D)** Metabolic alkalosis with respiratory acidosis
- **E)** Mixed metabolic and respiratory alkalosis

Answer

Correct answer : Mixed metabolic and respiratory alkalosis

To begin the interpretation, the patient has an alkalosis as reflected by the high pH. The bicarbonate is high indicating a metabolic alkalosis but she is also hypoxic with a lowish pCO2. This suggests a combined metabolic and respiratory alkalosis. This picture could be found in association with lung disease and prolonged vomiting.

Question 31

A 15 year old male is investigated for fatigue. His academic performance is also very poor being in the remedial class. Examination is normal with a pulse of 68 bpm and blood pressure of 106/70 mmHg. Investigations reveal:
Analysis of a blood and a 24 hour urine collection reveals:

		Normal Ranges
Sodium	140 mmol/L	(135-145)
Potassium	2.9 mmol/L	(3.5-5)
Urea	5.0 mmol/L	(3-8)
Bicarbonate	36 mmol/L	(20-28)
Random Glucose	4.5 mmol/L	(3.0-6.0)
Potassium	266 mmol/24h	(25-100)
Sodium	92 mmol/24h	(100-250)
Serum Magnesium	0.9 mmol/L	(0.7-1.2)

Which of the following is the likely diagnosis?

- **A)** Bartter syndrome
- **B)** Conn's syndrome
- **C)** Gitelman syndrome
- **D)** Liddle's syndrome
- **E)** Renal artery fibromuscular dysplasia

Answer

Correct answer : Bartter syndrome

The patient has a hypokalemic metabolic alkalosis with urinary potassium wasting, a normal blood pressure and in the context of poor academic performance is likely to have Bartter syndrome. The normal blood pressure makes Conn's, fibromuscular dysplasia and Liddle's unlikely. Bartter's syndrome usually presents in childhood with polyuria, nocturnal enuresis and growth retardation. Bartter's syndrome is associated with hyperplasia of the juxtaglomerular apparatus. The normal serum magnesium makes it more likely to be Barrter's vs Gitelman's

Question 32

A 24 year old who was involved in a car crash 4 days ago, is presently being nursed in high dependency unit. His general physical and systemic examination is unremarkable. The recent biochemistry results are as shown below:

		Normal Ranges
Sodium	119 mmol/L	(135-145)
Potassium	3.8 mmol/L	(3.5-5.5)
Urea	18.3 mmol/L	(3-8)
Creatinine	115 µmol/L	(60-115)
Calcium	2.65 mmol/L	(2.2-2.6 mmol/L)
TSH	2.24 mU/L	(0.35-5.5 mU/L)
Free T^4	16.9 pmol/L	(11.5-22.7 pmol/L)
Prolactin	480 mU/L	%nbsp;
Glucose	6.3 mmol/L	%nbsp;
0 hour cortisol	404 nmol/L	%nbsp;
30 minute cortisol	780 nmol/L	(post 250 µg ACTH injection)
Serum osmolality	254 mOsm/Kg	%nbsp;
Urine osmolality	480 mOsm/Kg	%nbsp;
Urine spot Na	6 mmol/L	%nbsp;

What is the most appropriate next step in his management?

- **A)** Fluid restriction of 1.5 l/day
- **B)** Hypertonic normal saline 1 litre over 6 hours and repeat electrolytes
- **C)** Normal saline 1 litre over 6 hours and repeat electrolytes
- **D)** Start demeclocycline
- **E)** Start tolvaptan

Answer

Correct answer : Normal saline 1 litre over 6 hours and repeat electrolytes

This 24 year old appears slightly hypovolaemic (with raised urea and creatinine but has normal physical examination) and has hyponatraemia in the presence of normal thyroid and adrenal function (TFT/short synacthen test normal). We are not told that he has any acute presentation with the hypovolaemia and as he has been in ITU for 4 days one might well assume that this is chronic hyponatraemia. The serum osmolality is low with low levels of sodium excretion from the urine (in contrast to syndrome of inappropriate antidiuretic hormone secretion (SIADH) which is associated with low serum osmolality along with excessive urinary sodium loss- >20 mmol/L). As a result the patient would benefit from fluid replacement and the rechecking of his electrolyte levels. There is no urgency here for hypertonic saline as per the european guidelines.

Question 33

According to NICE guidelines, which of the following oral hypoglycaemic agent is safe to use in women with gestational diabetes in pregnancy?

- **A)** Acarbose
- **B)** Gliclazide
- **C)** Glibenclamide
- **D)** Pioglitazone
- **E)** Sitagliptin

Answer

Correct answer : Glibenclamide

According to NICE guidelines on diabetes and pregnancy (NICE Clinical guidelines 63), glibenclamide is a safe agent to be used in women with gestational diabetes. The other agents which can be used safely in pregnancy include:

- Metformin
- Rapid acting insulin analogues such as aspart and lispro
- Isophane insulin (NPH)

Question 34

A 17 year girl with a history of sensorineural hearing loss and primary hypothyroidism presents to the clinic with primary amenorrhoea. She is 148 cm tall with a bodyweight of 60 Kg. She has widely spaced nipples and cubitus valgus on examination. Her uterus is small on ultrasound with the left kidney not visualised. What is the likely underlying diagnosis?

- **A)** Alport syndrome
- **B)** Congenital adrenal hyperplasia
- **C)** Mixed gonadal dysgenesis (XY mosaic)
- **D)** Polycystic ovarian syndrome
- **E)** Turner syndrome

Answer

Correct answer : Turner syndrome

The presence of primary amenorrhoea, short stature, thyroid and renal abnormalities noted in this girl, points towards the diagnosis of Turner syndrome, which is the most common X-chromosomal abnormality seen in females, with an incidence of 1:2500 live female births. It is associated with premature ovarian failure in 90% of affected patients.

The characteristic phenotypic features include - short stature, webbed neck, high arched palate, cubitus valgus, epicanthal folds and widely spaced nipples. The associated abnormalities include coarctation of the aorta, hypothyroidism, lymphoedema, coeliac disease, chronic liver disease and rheumatoid arthritis. The management includes growth hormone replacement till the final height is reached and life-long oestrogen replacement therapy.

Question 35

What's the likely mode of action of carbimazole?

- **A)** Inhibition of the sodium - iodide symporter
- **B)** Inhibition of thyroid peroxidase activity
- **C)** Inhibition of conversion of T^4 to T^3
- **D)** Inhibition of TBG
- **E)** Inhibition of TSH receptors

Answer

Correct answer : Inhibition of thyroid peroxidase activity

Carbimazole (CBZ) and propylthiouracil (PTU) act by inhibiting the action of thyroid peroxidase (TPO) enzyme. PTU in addition inhibits the peripheral conversion of T_4 to T_3 (by inhibition of 5^1 deiodinase type 1 activity). Perchlorate and thiocyanates inhibit iodide transport.

Question 36

A 16 year old with a past medical history of idiopathic growth hormone deficiency is reviewed in the transition clinic. He has been on growth hormone (GH) replacement therapy for the last 7 years. His insulin tolerance test (ITT), done after discontinuation of GH injections for 4 weeks, show a GH response of > 25 mU/L. What is the most appropriate step in his further management?

- **A)** Check IGF-1 levels
- **B)** Check IGFBP 3 levels
- **C)** Continue growth hormone injections
- **D)** Reassess the growth hormone secretion in 6 months
- **E)** Reassure and discharge

Answer

Correct answer : Reassure and discharge

In a child with idiopathic growth hormone deficiency diagnosed in childhood, the growth hormone axis should be reassessed on transition to adulthood as a spontaneous remission can be seen in a number of such children. The gold standard for assessment of GH secretion remains insulin tolerance test (ITT) in the absence of contraindications for the test. GH levels of <3 µg/L (<10 mU/L) are usually indicative of severe GH deficiency. This 16 year old is showing adequate growth hormone secretion on ITT, as a result his therapy can be safely discontinued.

Question 37

MEN-2 syndrome is associated with

- **A)** Activating mutation of RET proto-oncogene
- **B)** Inactivating mutation of RET proto-oncogene
- **C)** MENIN mutation
- **D)** NF-1 mutation
- **E)** VHL mutation

Answer

Correct answer : Activating mutation of RET proto-oncogene

MEN- 2 syndrome is an autosomal dominant condition due to a mutation in the RET proto-oncogene located on chromosome 10. RET is a single transmembrane domain comprising of an extracellular domain (which is cysteine rich) and an intracellular tyrosine kinase domain. MEN 2A is associated with an activating mutation of the extracellular cadherin like domain in contrast to MEN 2B which is associated with a mutation in the intracellular domain.

Question 38

A 44 year old undergoes bariatric surgery which leads to a 3 stone weight loss. 6 months postoperatively, while driving down a tunnel, he develops an inability to see clearly and narrowly misses having an accident.

Which is the likely mineral/vitamin deficiency contributing to his visual impairment?

- **A)** Copper
- **B)** Vitamin A
- **C)** Vitamin B6
- **D)** Vitamin B12
- **E)** Zinc

Answer

Correct answer : Vitamin A

Vitamins A and D are fat soluble vitamins which may be deficient in patients who undergo bariatric surgery and develop malabsorption during the postoperative phase. The shortening of length of the bowel and dumping syndrome contribute to the process of malabsorption. Vitamin A deficiency is associated with night blindness, xerophthalmia and occasionally complete blindness (Vitamin A deficiency being one of the leading preventable causes of blindness in developing countries). Night blindness usually manifests as an inability in adjustment to dimmed light and is an early feature of Vitamin A deficiency. The production of eye pigment - rhodopsin (found in the retina), which is responsible for sensing low light situations is impaired in Vitamin A deficiency.

Question 39

A 42-year-old male is admitted with a two-hour history of central abdominal pain that radiates into the back and vomiting. He has a background of type 2 diabetes and takes atorvastatin and metformin. On examination, his temperature is 37.8^{o}C, his pulse is 102 bpm reg, blood pressure 122/74 mmHg and oxygen saturations are 96% on air. He has central abdominal guarding with no palpable masses.

Investigations reveal normal FBC, Normal U+Es, CRP 102 mg/dl (<5) and an amylase of 980 u/l (50-110) and glucose 10.8 mmol/l (3.5-5.5). his lipid profile shows cholesterol of 10.8 mmol/l and a triglyceride of 40.8 mmol/l (0.9-1.5).

He is considered to have a diagnosis of pancreatitis and is treated with iv fluids, ng tube suction and analgesia.

Which of the following is the most appropriate approach to the management of this patient?

- **A)** Add gemfibrozil
- **B)** Add omega-3 fatty acids
- **C)** Commence fixed-dose insulin infusion
- **D)** Commence haemodialysis
- **E)** Commence sliding scale insulin

Answer

Correct answer : Commence fixed-dose insulin infusion

Explanation:

This man has pancreatitis associated with severe hypertriglyceridaemia. He is receiving appropriate treatment for the pancreatitis and requires a fixed-dose insulin regime rather than insulin sliding scale to reduce the hypertriglyceridaemia. A higher dose of insulin is required to drive lipoprotein lipase activity and reduce triglycerides which differs from a sliding scale where the insulin is tapered at low glucose. Even if this patient were to have normal glucose then a fixed-dose insulin regime would be the appropriate treatment.

Apheresis (not hemodialysis) has been considered as an approach to the treatment of hypertriglyceridaemia in conjunction with pancreatitis but there is no hard evidence to support this.

Reference:

- Ewald, N. and Kloer, H.U., 2012. Treatment options for severe hypertriglyceridemia (SHTG): the role of apheresis. Clinical research in cardiology supplements, 7(1), pp.31-35.

Question 40

A 31 year old woman who is 11 weeks pregnant presents with tachycardia, tremors and palpitations. She has a strong family history of autoimmune thyroid disease and goitre. Her thyroid function test results are as shown below:

		Normal Ranges
Free T_4	32.8 pmol/L	(9-23)
Free T_3	11.2 pmol/L	(3.5-6.5)
TSH	< 0.01 mU/L	(0.35-5.5)

What is the best therapeutic option in her case?

- **A)** Carbimazole
- **B)** Lugols iodine
- **C)** Propranolol
- **D)** Propylthiouracil
- **E)** Radioiodine

Answer

Correct answer : Propylthiouracil

The patient is likely to have Graves' thyrotoxicosis as suggested by features of hyperthyroidism and an associated strong family history of autoimmune thyroid disease. In view of her pregnant state, treatment with lowest dose of propylthiouracil, which renders her euthyroid, should be initiated. The following are a few salient points to be remembered as far as pregnancy and thyroid dysfunction is concerned:

- Thyroxine requirements increase in hypothyroid women during the first trimester of pregnancy.
- TSH levels increase during the 2^{nd} and 3^{rd} trimesters of pregnancy.
- Hyperthyroidism in pregnancy is commonly due to Graves' disease (d/d hyperemesis gravidarum, H mole), so check TSH receptor antibodies (TRAb) in all such patients.
- Graves' disease can relapse during first trimester and postpartum period (more likely to remit during 2^{nd} and 3^{rd} trimester)
- Check TRAb in the third trimester, as it can be transmitted through the placenta to the baby, leading to neonatal hyperthyroidism
- Treat maternal hyperthyroidism with the lowest possible dose of PTU (more protein bound, less transfer across placenta)
- 1 out of 4 type 1 diabetics, have evidence of thyroid dysfunction during pregnancy

Question 41

A 54 year old man attends for clinical assessment. He sustained an MI at the age of 40, but is now clinically stable with no cardiovascular symptoms. His lipid profile is well controlled on a combination of atorvastatin 80 mg once daily and ezetimibe 10 mg once daily. He also takes ramipril 10 mg once daily and aspirin 75 mg once daily. He has seen a specialist privately, who has advised him that he has ‘possible familial hypercholesterolaemia (FH)’ based upon his history and lipid results. He recommends that his children, now aged 20 and 24 have ‘appropriate testing’. The patient has read that genotyping is advised in individuals with FH, but is concerned as the specialist indicated that this test was not available locally. What is the most appropriate advice with respect to genetic testing?

- **A)** DNA testing is not required for him but is obligatory for his children
- **B)** DNA testing is obligatory for him, but is not required for his children
- **C)** Genetic testing is not required as the risk of his children inheriting the same condition as him is very unlikely
- **D)** His children should be started on a statin regardless of any further testing
- **E)** In the absence of DNA testing, his children should be offered lipid testing

Answer

Correct answer : In the absence of DNA testing, his children should be offered lipid testing

Genetic testing for FH is desirable to confirm the diagnosis and facilitate cascade testing in his relatives. Testing is not universally available in the UK or elsewhere in the world, although its use is recommended within NICE guidance. If he were found to have an FH causing mutation, family members should be offered testing to ascertain if the family mutation is present. Lipid testing and potentially treatment should be organised thereafter. In the absence of genetic testing a clinical diagnosis can be made and lipid testing offered to family members.

Further Reading

NICE CG71 (2008) Identification and management of familial hypercholesterolaemia for familial hypercholesterolaemia

Question 42

A 35 year old doctor seeks your advice as he has a family history of heart disease and has been found to have high cholesterol following tests carried out for a clinical trial. He is very fit and undertakes regular triathlons. He takes no medication, is a non-smoker and teetotal. He is fastidious about maintaining a healthy diet. You ascertain that his father, who is also a non-smoker and generally fit, sustained a non-fatal myocardial infarction (MI) at the age of 44. A paternal uncle sustained a fatal MI at the age of 53. He has no stigmata of hyperlipidaemia, his blood pressure is 118/76 mmHg and has a waist circumference of 80 cm and a BMI of 23 kg/m^2.

His lipid profile measurements are:-

	Results	Reference interval
Total cholesterol	9.8 mmol/L	
HDL cholesterol	1.3 mmol/L	>1.0
Triglycerides	5.7 mmol/L	<2.0
Calculated LDL	Unable to calculate	
Fasting glucose	4.6 mmol/L	3.0-6.0
Thyroid profile	normal	
HbA1c	35 mmol/mol	<48
Apolipoprotein B	1.9 g/L	0.4-1.2

Which of the following is the most likely diagnosis?

- **A)** Anabolic steroid misuse
- **B)** Familial combined hyperlipidaemia
- **C)** Familial hypercholesterolaemia
- **D)** Lipoprotein lipase deficiency
- **E)** Polygenic hypercholesterolaemia

Answer

Correct answer : Familial combined hyperlipidaemia

Familial combined hyperlipidaemia (FCH) is a commonly encountered hyperlipidaemia and is associated with premature cardiovascular disease. Unlike familial hypercholesterolaemia, the genetics of the condition are not clear and the presentation much more variable. Whilst obesity and insulin resistance are more commonly associated with FCH, this is not invariably the case. The commonest laboratory findings are raised cholesterol and triglycerides (i.e. combined), together with a raised concentration of apolipoprotein B. This is the surface protein present on both very low density lipoproteins (VLDL) as well as low density lipoprotein (LDL) and is a good marker of atherosclerotic risk. Both familial and polygenic hypercholesterolaemia are less commonly associated with hypertriglyceridaemia in the absence of diabetes mellitus, obesity or alcohol excess. Anabolic steroid misuse usually causes low HDL cholesterol. Lipoprotein lipase deficiency is very rare, is usually associated with a more severe dyslipidaemia and is inherited in an autosomal recessive manner, which is not consistent with his family history.

Further Reading

Heart UK Familial Combined Hyperlipidaemia (FCH)

Larry A. Weinrauch, LA (MD) MedlinePlus Medical Encyclopedia (2014) Familial combined hyperlipidaemia

Question 43

A 15 year old boy attends clinic with his mother. The mother has just been diagnosed with familial hypercholesterolaemia (FH). She has a strong family history of premature cardiovascular disease and was found to have significant hypercholesterolaemia. She recently had a genetic test carried out and has been advised that a mutation in the LDL receptor causing FH has been identified. She has been advised that on this basis, ‘cascade testing’ of her family should be undertaken. She seeks your advice about cascade testing and what should be done now:

- **A)** Cascade testing using DNA is not appropriate as LDL receptor mutations are very rare and full gene sequencing of the son is required
- **B)** Offer a cholesterol test to her son and her other family members to assess if hypercholesterolaemia is present in them before offering a DNA test
- **C)** Offer a DNA test to adult family members and a cholesterol test in family members aged between 8 and 16 years old
- **D)** Offer a DNA test to adult family members only to assess if the identified mutation is present in them before offering a cholesterol test
- **E)** Offer a DNA test to her son and her other family members to assess if the identified mutation is present in them before offering a cholesterol test

Answer

Correct answer : Offer a DNA test to her son and her other family members to assess if the identified mutation is present in them before offering a cholesterol test

Individuals who have a high clinical probability of having FH should be offered genotyping. This can confirm the diagnosis, but importantly can facilitate cascade testing. Once the DNA mutation has been identified in the presenting patient (known as the ‘index’ patient), testing for the presence or absence of this specific mutation can be undertaken in family members. This is carried out in a step wise fashion, such that first degree relatives i.e. parents, children and siblings are tested first and subsequent relatives thereafter. For example if the index patient’s brother does not have the mutation, testing in his children is not required. If the index patient’s sister does have the mutation, her children will be offered testing.

Offering DNA testing, rather than initial cholesterol testing in family members is recommended, as it provides a definitive answer, particularly in younger people when the cholesterol results may be harder to interpret. Cholesterol testing should be carried out in family members who have the family mutation, but in those who do not; this may not be required, particularly for children. DNA testing should be offered to children by the age of 10. LDL receptor mutations are the commonest cause of FH. Less commonly mutations are found in the apo B or PCSK9 genes.

Further Reading:

Heart UK Children and familial hypercholesterolaemia

Question 44

A 39 year old man previously fit and well is admitted to hospital with an acute myocardial infarction (MI). He is successfully treated with percutaneous coronary intervention. The admitting doctor notes that his father sustained a fatal MI at the age of 52 and his paternal grandfather sustained a fatal MI at the age of 48. On examination he is found to have xanthomata in both Achilles' tendons, bilateral corneal arcus and marked xanthelasma. His lipid profile is measured on admission:

	Results	Reference interval
Total cholesterol	11.2 mmol/L	
HDL cholesterol	1.3 mmol/L	>1.0
Triglycerides	1.5 mmol/L	<2.0
Calculated LDL	9.2 mmol/L	
Fasting glucose	5.2 mmol/L	3.0-6.0
Thyroid profile	normal	

The following clinical findings are relevant for the diagnosis of familial hypercholesterolaemia:

- **A)** Premature corneal arcus is pathognomonic of FH and confirms the diagnosis
- **B)** Premature marked xanthelasma are pathognomonic of FH and confirm the diagnosis
- **C)** Tendon xanthomata are pathognomonic of FH and confirm the diagnosis
- **D)** The clinical findings are not relevant as the LDL is >7.9 mmol/L, which confirms the diagnosis
- **E)** The diagnosis may only be confirmed with a DNA test

Answer

Correct answer : Tendon xanthomata are pathognomonic of FH and confirm the diagnosis

Tendon xanthomata are pathognomonic of FH and confirm the diagnosis. These may manifest as thickening and/or hardening of tendons, usually associated with distinct nodularity. They are commonly found in the Achilles' tendons and sometimes in other extensor tendons, such as those of the hands. The presence of xanthelasma and premature arcus are suggestive, but are not specific for FH. Xanthelasma may be found in the absence of hypercholesterolaemia, but its finding should prompt measurement of a lipid profile. Corneal arcus becomes more common with advancing age, but it's presence in a person under the age of 40 is suggestive of a lipid disorder. The probability of FH increases with higher LDL cholesterols, but there is no definitive diagnostic cut-off above which the diagnosis is confirmed. A DNA test may confirm the diagnosis, but the patient may be described as having definite FH in the presence of the above profile with xanthoma.

Further Reading

NICE guidelines CG71 (2008) Identification and management of familial hypercholesterolaemia

FH Wales Clinical signs of familial hypercholesterolaemia

Question 45

An 11 year old boy attends clinic with his mother. The boy's father has just died of a myocardial infarction at the age of 32 and the mother is concerned. The boy has a paternal uncle who also developed premature ischaemic heart disease at a young age and is reported to have had a total cholesterol of 11.5 mmol/L before treatment. Her son has now had his lipid profile measured.

	Results	Reference interval
Total cholesterol	6.5 mmol/L	
HDL cholesterol	1.3 mmol/L	0.8-1.9
Triglycerides	1.2 mmol/L	0.5-2.2
Calculated LDL	4.7 mmol/L	
Fasting glucose	4.8 mmol/L	3.0-6.0

The following next step would be the most appropriate:

- **A)** Advise that the diagnosis of familial hypercholesterolaemia can only be made with a DNA test
- **B)** He and the mother should be reassured that the lipids are unremarkable
- **C)** Offer annual testing of the lipid profile through puberty
- **D)** The lipid profile should be re-checked when he is an adult
- **E)** The results suggest familial hypercholesterolaemia and a specialist referral is appropriate

Answer

Correct answer : The results suggest familial hypercholesterolaemia and a specialist referral is appropriate

Cholesterol is lower in children than in adults and the results in the context of the history are suggestive of familial hypercholesterolaemia (FH). Assessment within a specialist paediatric setting is appropriate. In FH, ideally the diagnosis should be made by testing for the known family DNA mutation, but if this is neither known nor available, lipid testing is appropriate. Deferring the diagnosis with such a concerning family history is undesirable. Statins may be used in children from the age of 10.

Further Reading

NICE guidelines CG71 (2008) Identification and management of familial hypercholesterolaemia

HEART UK- the cholesterol charity Children and familial hypercholesterolaemia (FH)

FH Wales- website for the FH service in Wales, which offers a comprehensive clinical and family testing service

Question 46

A 32 year old man attends clinic asking for advice as his older brother has recently had a myocardial infarction at the age of 40. He is concerned as his symptoms, which he thinks are due to indigestion are getting worse. His father died of an MI at the age of 43. He is a very fit non-smoker, and has a healthy diet. He has gastro-oesophageal reflux, for which he takes omeprazole. Physical examination is normal with a blood pressure of 130/78 mmHg. You organise investigations with the following results:

	Results	Reference interval
Total cholesterol	9.7 mmol/L	
HDL cholesterol	1.5 mmol/L	>1.0
Triglycerides	0.6 mmol/L	<2.0
Calculated LDL	7.9 mmol/L	
Fasting glucose	4.8 mmol/L	3.0-6.0
Liver profile	normal	

Which of the following is the most likely diagnosis?

- **A)** Familial hypercholesterolaemia
- **B)** Hypercholesterolaemia secondary to diet
- **C)** Hyperlipidaemia secondary to myocardial ischaemia
- **D)** Hypothyroidism
- **E)** Polygenic hypercholesterolaemia

Answer

Correct answer : Familial hypercholesterolaemia

Heterozygous familial hypercholesterolaemia (FH) is estimated to affect 1 in 500 of the population and causes significantly elevated LDL cholesterol from birth. It is inherited in an autosomal dominant fashion, meaning that for any individual with the condition 50% of relatives will be affected. If untreated it is estimated that 50% of men will develop cardiovascular disease by the age of 60, but lipid lowering therapies are very effective at reducing this risk. As he has symptoms which may be due to myocardial ischaemia, this requires further evaluation, despite his youth. The family and personal history indicate that diet, polygenic causes and thyroid dysfunction are less likely. Total cholesterol is often lower following a myocardial infarction.

Further reading:

NICE CG71 (2008) Identification and management of familial hypercholesterolaemia

Heart UK (2015) What is Familial Hypercholesterolaemia (FH)?

FH Wales- information from a service which offers comprehensive clinical and family testing

AS04 : H·E·A·R·T UK Advice sheet diagnosing FH- Simon Broome Criteria

Question 47

A 37 year old man attends for evaluation due to his family history of premature vascular disease and is advised that he should have his lipid profile checked. He asks if fasting will make a difference to the results of the test.

What is the relevance of fasting status in the interpretation of a lipid profile?

- **A)** All the parameters within a lipid profile are significantly affected by fasting status
- **B)** Fasting is only relevant for the assessment of an apolipoprotein profile
- **C)** The equation used to calculate triglycerides is not applicable if the patient is not fasting
- **D)** Total cholesterol and HDL cholesterol only are affected by fasting status
- **E)** Triglycerides and calculated LDL cholesterol only may be affected by fasting

Answer

Correct answer : Triglycerides and calculated LDL cholesterol only may be affected by fasting

Most laboratories **measure** total cholesterol, HDL cholesterol and triglycerides and **calculate** LDL cholesterol by using the following formula (all parameters in mmol/L):

LDL cholesterol= total cholesterol- HDL cholesterol- (triglycerides/2.2) Triglycerides can increase in the non-fasting state and therefore also affect calculated LDL cholesterol. Current NICE guidance recommends using non fasting parameters such as non-HDL cholesterol (i.e. total cholesterol -HDL cholesterol) as these parameters are less affected by fasting status. Using a calculated LDL value can still be helpful for the assessment of familial hypercholesterolaemia.

The above equation is not applicable when the triglycerides are >4.4 mmol/L

Further reading

Joint British Society (2014) guidelines on prevention of cardiovascular disease 3

NICE guideline CG181 (2014) Lipid modification: cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease

Question 48

A 42 year old lady attends clinic complaining of persistent lethargy. She works as a teacher and is generally well. She has no relevant medical history and takes no regular medication. Her mother developed angina at the age of 75 and her father has no medical problems at the age of 78. On examination her pulse is 56 bpm, blood pressure is 122/72 mmHg, BMI of 26 kg/m^2 with no other obvious findings. Investigations reveal:

	Results	Reference interval
Total cholesterol	11.0 mmol/L	
HDL cholesterol	1.2 mmol/L	>1.2
Triglycerides	1.1 mmol/L	<2.0
Calculated LDL	9.3 mmol/L	
Fasting glucose	4.8 mmol/L	3.0-6.0
Creatine kinase	1350 u/L	25-200

Which of the following is the most likely diagnosis?

- **A)** Familial hypercholesterolaemia
- **B)** Hypercholesterolaemia secondary to diet
- **C)** Hyperlipidaemia secondary to skeletal muscle damage
- **D)** Hypothyroidism induced hypercholesterolaemia
- **E)** Polygenic hypercholesterolaemia

Answer

Correct answer : Hypothyroidism induced hypercholesterolaemia

Untreated hypothyroidism can cause a significant secondary hypercholesterolaemia, as thyroid hormones are involved with hepatic lipid metabolism. Secondary causes of dyslipidaemia should always be considered and include medications, alcohol, obesity, obstructive liver disease and nephrotic syndrome. Inherited causes of dyslipidaemia are less likely in the absence of a relevant family history. A raised creatine kinase is a relatively common finding in hypothyroidism, but is unrelated to the hypercholesterolaemia. Inappropriate diet alone rarely causes such a profound hypercholesterolaemia.

Further Reading

- GP notebook (2015) links to examples of secondary causes of hyperlipidaemia - UK Medical Reference

Question 49

A 52 year old man with familial hypercholesterolaemia (FH) and a previous myocardial infarction 3 years ago attends for review. He recalls a pretreatment total cholesterol of 8.0 mmol/L, but no other details are available. He has had difficulty tolerating a statin due to troublesome muscle pain. His symptoms settle following discontinuation of therapy but return within a week of recommencement. His serum creatine kinase has always been within the reference range. You have tried to use the following drug therapies, using the minimum dose indicated in the BNF: simvastatin, atorvastatin and rosuvastatin. He has tolerated pravastatin 40 mg once daily. His current biochemistry:

	Results	Reference interval
Total cholesterol	5.9 mmol/L	
HDL cholesterol	1.0 mmol/L	>1.0
Triglycerides	1.6 mmol/L	0.1-2.0
Calculated LDL	4.2 mmol/L	
Creatinine	125 mmol/L	70-120
eGFR	54 mL/min/ 1.73 m^2	>90

What would be the most appropriate next step to manage his lipid profile?

- **A)** Add ezetimibe 10 mg once daily
- **B)** Add fenofibrate 160 mg once daily
- **C)** Increase pravastatin to 80 mg once daily
- **D)** Prescribe coenzyme Q10
- **E)** Start lipoprotein apheresis immediately

Answer

Correct answer : Add ezetimibe 10 mg once daily

This patient is at high risk of recurrent cardiovascular events. NICE guidelines for FH recommend achieving a 50% reduction in cholesterol from the baseline measurement, which would be a reasonable initial target for this patient. Ezetimibe can effectively reduce LDL cholesterol by blocking intestinal absorption of dietary and biliary cholesterol, particularly in conjunction with a statin. Fenofibrate have a limited effect in reducing LDL cholesterol and should be used with caution in renal dysfunction, particularly in conjunction with a statin. Use of coenzyme Q10 to prevent statin induced myalgia is currently not recommended. He may be a candidate for lipoprotein apheresis, which is a treatment akin to renal dialysis for hypercholesterolaemia. All available drug therapies should be explored first as access to apheresis in the UK is limited and is costly. The maximum recommended dose of pravastatin is 40 mg once daily.

Further Reading

NICE guidelines CG71 (2008) Identification and management of familial hypercholesterolaemia for familial hypercholesterolaemia

NICE guideline CG181 (2014) Lipid modification: cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease

HEART UK What is LDL-apheresis?

Question 50

A 66 year old lady attends for routine review of her hypertension. She is fit and well with no other medical history. She takes perindopril 8 mg once daily for her hypertension, is a non-smoker and drinks about 10 units of alcohol per week. Her mother is alive at the age of 91, is in a nursing home with Alzheimer's disease, but has no history of vascular disease. Her father died at the age of 84 from carcinoma of the prostate. He also had treated hypertension, but had no history of vascular disease. She does not know of any family history of hyperlipidaemia or premature cardiovascular disease. Her blood pressure is well controlled. She has superior corneal arcus but no other physical signs and has a BMI of 22 kg/m^2. As part of a cardiovascular risk assessment she had a lipid profile requested 5 years ago and repeated last month.

5 years ago

	Results	Reference interval
Total cholesterol	7.3 mmol/L	
HDL cholesterol	1.9 mmol/L	>1.0
Triglycerides	1.8 mmol/L	<2.0
Calculated LDL	4.6 mmol/L	
Fasting glucose	5.2 mmol/L	3.0-6.0
Thyroid profile	normal	

Last month

	Results	Reference interval
Total cholesterol	7.7 mmol/L	
HDL cholesterol	1.8 mmol/L	>1.0
Triglycerides	1.8 mmol/L	<2.0
Calculated LDL	5.1 mmol/L	
Fasting glucose	5.4 mmol/L	3.0-6.0
Thyroid profile	normal	

eGFR	>90	>90
Urine protein: creatinine	<30 mg/mmol	<30 mg/mmol

The most likely diagnosis explanation for her lipid profile is:

- **A)** Drug-induced hyperlipidaemia
- **B)** Familial combined hyperlipidaemia
- **C)** Familial hypercholesterolaemia
- **D)** Polygenic hypercholesterolaemia
- **E)** Secondary hyperlipidaemia due to hypertension- induced nephropathy

Answer

Correct answer : Polygenic hypercholesterolaemia

Polygenic hypercholesterolaemia is a common finding, but unlike familial hypercholesterolaemia (FH) the genetics of the condition are less distinct. The hypercholesterolaemia often deteriorates over time and may be associated with cardiovascular disease, particularly in the context of other risk factors. The impact of polygenic hypercholesterolaemia in terms of atherogenesis is likely to be less significant than FH, bearing in mind that an individual with FH will have been exposed to high levels of atherogenic lipoproteins from birth, rather than just later in life. The absence of a family history makes FH and familial combined hyperlipidaemia less likely. ACE inhibitors do not cause a dyslipidaemia and there is no evidence of nephropathy in this patient.

Further Reading

General Practice Notebook Polygenic hypercholesterolaemia

Question 51

A 38 year old woman is 20 weeks pregnant and has her lipid profile tested at a private antenatal clinic because she has worried about heart disease in pregnancy since reading about this in a woman's magazine. She has no history or symptoms suggestive of cardiovascular disease. She informs you that her anxiety has been heightened as her father had a stroke at the age of 72 and her mother developed angina at the age of 70. The pregnancy is progressing well and her blood pressure is 110/68 mmHg. At 7 weeks gestation her weight was 54 kg, BMI 22 kg/m^2.

	Results	Reference interval
Total cholesterol	7.1 mmol/L	
HDL cholesterol	1.7 mmol/L	>1.0
Triglycerides	1.1 mmol/L	0.1-2.0
Calculated LDL	4.9 mmol/L	
Fasting glucose	5.0 mmol/L	3.5-5.5

Which of the following diagnoses is the most likely?

- **A)** Analytical error due to pregnancy affecting binding protein metabolism
- **B)** Familial hypercholesterolaemia
- **C)** Hypothyroidism
- **D)** Nephrotic syndrome
- **E)** Pregnancy induced hyperlipidaemia

Answer

Correct answer : Pregnancy induced hyperlipidaemia

Pregnancy can cause an oestrogen-mediated significant increase in cholesterol and measurement is best avoided during pregnancy. Relatives developing heart disease at an older age is less suggestive of an inherited dyslipidaemia.This patient can be reassured that her risk of developing cardiovascular disease in pregnancy is very low and that no further assessment is required.

Further Reading:

Metabolic changes during pregnancy

Question 52

A 64 year old man is reviewed 3 months following admission with a myocardial infarction. He required coronary artery bypass surgery but has made a good recovery and is asymptomatic. He is a life-long non-smoker, has had treated hypertension for 10 years and plans to return back to work on a part-time basis. His lipid profile prior to his MI reveals:

	Results	Reference interval
Total cholesterol	5.7 mmol/L	
HDL cholesterol	1.0 mmol/L	>1.0
Triglycerides	0.8 mmol/L	0.1-2.0
Calculated LDL	4.3 mmol/L	
Fasting glucose	4.8 mmol/L	3.5-5.5

He has never taken a statin because of concerns about side-effects and has not started the atorvastatin recommended by his cardiac surgeon. Which of the following actions is appropriate?

- **A)** Advise that dietary measures alone are appropriate and refer to a dietitian
- **B)** Advise that statin therapy is safe in nearly all people and is recommended for all patients following CABG
- **C)** Recommend a bile acid sequestrant
- **D)** Recommend starting a fibrate
- **E)** Recommend starting ezetimibe

Answer

Correct answer : Advise that statin therapy is safe in nearly all people and is recommended for all patients following CABG

Lipid lowering with a statin is recommended for all patients who have established cardiovascular disease (secondary prevention). In an individual who has never experienced side-effects, he should be reassured that statins are safe and effective at reducing the risk of recurrent cardiovascular events. Risk factor calculators are not appropriate for use in secondary prevention. Dietary advice is an important adjunct to drug therapy in this situation, but not as the only intervention. Drug therapies, other than statins should not be offered at this stage as monotherapy.

Further Reading:

- Hypercholesterolaemia- secondary prevention
- NICE CG 181

Question 53

A 52 year old man attends for a cardiovascular risk assessment. He is not concerned about his health, but his wife has mentioned that he has gradually put on weight over the last few years and should have a check up. He is generally well with no family history of premature vascular disease. He carries out little physical activity and is a non-smoker. The following are results from your assessment.

	Results	Reference interval
Blood pressure	160/95	
Weight	105 kg	
BMI	33 kg/m^2	
Total cholesterol	7.4	
HDL cholesterol	0.8	>1.0
Triglycerides	2.4	0.1-2.0
Calculated LDL	5.5	
Fasting glucose	5.4	3.5-5.5
HbA1c	36	20-42

His calculated 10 year cardiovascular risk (QRISK2) is 34%. He is started on atorvastatin 20 mg once daily, which is gradually up titrated to 80 mg once daily, and ramipril 5 mg once daily. Twelve months later his parameters are as follows:

	Results	Reference interval
Blood pressure	145/95	nbsp;
Weight	106 kg	nbsp;
BMI	33 kg/m^2	nbsp;
Total cholesterol	3.7	nbsp;
HDL cholesterol	0.8	>1.0
Triglycerides	2.3	0.1-2.0

Calculated LDL	1.9	nbsp;
Fasting glucose	5.2	3.5-5.5
HbA1c	35	20-42

The following is the next most appropriate management step

- **A)** Add a fibrate
- **B)** Consider HDL raising therapy
- **C)** Increase dose of statin
- **D)** No change, monitor annually
- **E)** Reinforce diet and lifestyle advice

Answer

Correct answer : Reinforce diet and lifestyle advice

This gentleman is offered treatment in the context of primary prevention. Pharmacological intervention is appropriate, but there are no specific ‘lipid targets’. The current guidance for lipid modification from NICE recommends offering intervention if CV risk is greater than 10% over 10 years. His hypertriglyceridaemia and low HDL cholesterol are related to obesity and lifestyle intervention and will provide the greatest opportunity for health improvement. Clinical trials are underway with specific HDL raising drugs to ascertain their safety and potential utility.

Further Reading:

- Joint British Society guidelines on prevention of cardiovascular disease 3 (2014)
- NICE CG181

Question 54

A 33 year old woman is discharged from the surgical ward following acute admission with abdominal pain and a diagnosis of acute pancreatitis, this settled with conservative management. She drinks no alcohol, has no relevant medical history and takes no medication. Her hepatic ultrasound shows no evidence of gallstones. On admission the surgical team had checked a fasting lipid profile and ask you to follow up on the results below:

	Results	Reference interval
Total cholesterol	12.1 mmol/L	
HDL cholesterol	0.6 mmol/L	>1.0
Triglycerides	45 mmol/L	0.1-2.0
Calculated LDL	unable to calculate due to high triglycerides	
Fasting glucose	4.8 mmol/L	3.5-5.5

Which of the following actions would be the most appropriate?

- **A)** Introduce no new medication
- **B)** Prescribe a fibrate
- **C)** Prescribe a statin
- **D)** Prescribe ezetimibe 10 mg once daily
- **E)** Prescribe omega 3 fatty acids g once daily

Answer

Correct answer : Prescribe a fibrate

Hypertriglyceridaemia can cause pancreatitis, and in this situation, drug therapy to reduce triglycerides is appropriate. The most effective group of agents for this are the fibrates. Statins and ezetimibe have a minimal effect on hypertriglyceridaemia. High dose (4 g/day) of omega 3 fatty acids can be helpful, often in conjunction with a fibrate; however at a low dose the impact on triglyceride metabolism is minimal. She is likely to have an underlying defect in triglyceride metabolism which will require further assessment.

Further Reading:

- Management of hypertriglyceridaemia

Question 55

A 41 year old man attends for a general medical review. He is under the care of the mental health team with schizophrenia which has been successfully treated with olanzapine for 2 years. He has smoked since adolescence and does not drink alcohol for religious reasons. His other medications include bendroflumethiazide and omeprazole. He was recently started on varenicline to help him stop smoking. There is no family history of premature vascular disease. He last attended your practice 3 years ago, when the following were measured.
Assessment and investigations 3 years ago:

	Results	Reference interval
Blood pressure	135/85 mmHg	
Weight	85 kg	
BMI	26 kg/m^2	
Total cholesterol	5.8 mmol/L	
HDL cholesterol	0.9 mmol/L	>1.0
Triglycerides	1.8mmol/L	0.1-2.0
Calculated LDL	4.1 mmol/L	
Fasting glucose	5.4 mmol/L	3.5-5.5

His most recent assessment reveals:

	Results	Reference interval
Blood pressure	145/85 mmHg	
Weight	95 kg	
BMI	30 kg/m^2	
Total cholesterol	7.0 mmol/L	
HDL cholesterol	0.7 mmol/L	>1.0
Triglycerides	3.2 mmol/L	0.1-2.0
Calculated LDL	4.7 mmol/L	

Fasting glucose	6.3 mmol/L	3.5-5.5
HbA1c	39 mmol/mol Hb	20-42

The most likely reason for the change in his metabolic parameters is

- **A)** Bendroflumethiazide induced dyslipidaemia
- **B)** Diabetes mellitus
- **C)** Lipoprotein lipase deficiency
- **D)** Olanzapine induced dyslipidaemia
- **E)** Varenicline induced dyslipidaemia

Answer

Correct answer : Olanzapine induced dyslipidaemia

Olanzapine and other atypical antipsychotic drugs can cause weight gain through increased appetite, as well as hyperglycaemia and hyperlipidaemia. Substitution of a more metabolically favourable drug is an option, but rarely happens in clinical practice, where dealing with the adverse metabolic consequences is the more usual course of action. The fasting glucose and HbA1c are consistent with impaired fasting glycaemia. The absence of a relevant family history make both familial combined hyperlipidaemia and the very rare condition lipoprotein lipase deficiency unlikely. Bendroflumethiazide can cause mild hypertriglyceridaemia, but not with this severity and it is rarely clinically significant.

Further reading:

- Dyslipidaemia and atypical antipsychotic drugs

Question 56

A 60 year old man with a three year history of diet controlled type 2 diabetes mellitus and a previous myocardial infarction (MI) 3 years ago attends for review. He stopped smoking at the time of his MI. He has had difficulty tolerating a statin due to troublesome muscle aches and pains. His symptoms settle following discontinuation of therapy but return within a week of recommencement. His serum creatine kinase has always been within the reference range. You have tried to use the following drug therapies, using the minimum dose indicated in the BNF: simvastatin, atorvastatin and rosuvastatin. He has tolerated pravastatin 40 mg once daily. His current biochemistry:

	Results	Reference interval
Total cholesterol	6 mmol/L	
HDL cholesterol	1.0 mmol/L	>1.0
Triglycerides	1.5 mmol/L	0.1-2.0
Calculated LDL	4.3 mmol/L	
Creatinine	125 mmol/L	70-120
eGFR	54 mL/min/ 1.73 m^2	>90

What would be the most appropriate next step to manage his lipid profile?

- **A)** Add ezetimibe 10 mg once daily
- **B)** Add fenofibrate 160 mg once daily
- **C)** Add omega 3 fatty acids
- **D)** Continue current therapy
- **E)** Increase pravastatin to 80 mg once daily

Answer

Correct answer : Add ezetimibe 10 mg once daily

This patient is at high risk of cardiovascular events due to diabetes mellitus, previous MI and smoking history. In this patient we are dealing with secondary prevention and the aim should be to reduce his LDL cholesterol, ideally to <2 mmol/L. The maximum recommended dose of pravastatin is 40 mg once daily. But even at maximum dose pravastatin is a low intensity statin, i.e. reduces LDL cholesterol by 29% from baseline. Ezetimibe can effectively reduce LDL cholesterol by blocking intestinal absorption of dietary and biliary cholesterol, particularly in conjunction with a statin. Both omega 3 fatty acids and fenofibrate have a limited effect in reducing LDL cholesterol. Fenofibrate should be used with caution in renal dysfunction, particularly in conjunction with a statin. NICE CG181 does not recommend fibrates or omega 3 fatty acids for the prevention of cardiovascular disease.

Further Reading:

- NICE guidelines for type 2 diabetes
- NICE technology appraisal for ezetimibe

Question 57

A 39 year old man attends clinic asking for advice as his older brother has recently had a myocardial infarction at the age of 44. His father died of an MI at the age of 43. He is a very fit non-smoker, and has a healthy diet. He runs about 10 miles weekly and has no symptoms whatsoever. He has no other medical problems or takes any medication. Physical examination is normal with a blood pressure of 120/68 mmHg. You organise investigations with the following results:

	Results	Reference interval
Total cholesterol	10.7 mmol/L	
HDL cholesterol	1.5 mmol/L	>1.0
Triglycerides	0.6 mmol/L	0.1-2.0
Calculated LDL	8.9 mmol/L	
Fasting glucose	4.3 mmol/L	3.5-5.5
Liver profile	normal	

Which of the following is the most likely diagnosis?

- **A)** Familial hypercholesterolaemia
- **B)** Hypercholesterolaemia secondary to diet
- **C)** Hyperlipidaemia secondary to alcohol excess
- **D)** Hypothyroidism
- **E)** Polygenic hypercholesterolaemia

Answer

Correct answer : Familial hypercholesterolaemia

Heterozygous familial hypercholesterolaemia (FH) is estimated to affect 1 in 500 of the population and causes significantly elevated LDL cholesterol from birth. It is inherited in an autosomal dominant fashion, meaning that for any individual with the condition 50% of relatives will be affected. If untreated it is estimated that 50% of men will develop cardiovascular disease by the age of 60, but lipid lowering therapies are very effective at reducing this risk. NICE guidelines for FH recommend treating with a statin and then ezetimibe if required.

Further Reading:

- NICE guidelines for familial hypercholesterolaemia
- HEART UK- the cholesterol charity- Information on FH for patients and healthcare professionals
- FH Wales- information from a service which offers comprehensive clinical and family testing
- http://www.fhservice.wales.nhs.uk/home

Question 58

A 50 year old man attends clinic. He works as a civil servant and is generally well. He has felt increasingly tired over the last year, but has attributed this to difficulties at work. He has also gained about 5 kgs in weight over the last six months. He has no relevant medical history, takes no regular medication and is physically active. Both of his parents are healthy octogenarians. His sister takes medication for her thyroid. On examination, his pulse is 56 bpm, blood pressure is 122/72 mmHg with no other obvious findings and he has a BMI of 28 kg/m^2. Investigations reveal:

	Results	Reference interval
Total cholesterol	10.0 mmol/L	
HDL cholesterol	1.2 mmol/L	>1.0
Triglycerides	1.1 mmol/L	0.1-2.0
Calculated LDL	8.3 mmol/L	
Fasting glucose	4.8 mmol/L	3.5-5.5

Which of the following is the most likely diagnosis?

- **A)** Familial hypercholesterolaemia
- **B)** Hypercholesterolaemia secondary to diet
- **C)** Hyperlipidaemia secondary to alcohol excess
- **D)** Hypothyroidism induced hypercholesterolaemia
- **E)** Polygenic hypercholesterolaemia

Answer

Correct answer : Hypothyroidism induced hypercholesterolaemia

Untreated hypothyroidism can cause a significant secondary hypercholesterolaemia, as thyroid hormones are involved with hepatic lipid metabolism. Secondary causes of dyslipidaemia should always be considered and include medications, alcohol, obesity, obstructive liver disease and nephrotic syndrome. Inherited causes of dyslipidaemia are less likely in the absence of a relevant family history. Dietary indiscretion alone rarely causes such a profound hypercholesterolaemia.

Further Reading:

Further reading on secondary causes of hyperlipidaemia

Question 59

A 55 year old man with chronic hyponatraemia associated with bronchial carcinoma is receiving treatment with tolvaptan. Which class of drug is tolvaptan?

- **A)** Aldosterone receptor agonist
- **B)** Sodium-potassium channel blocker
- **C)** Vasopressin receptor agonist
- **D)** Vasopressin receptor antagonist
- **E)** Vasopressinase analogue

Answer

Correct answer : Vasopressin receptor antagonist

Tolvaptan is a drug developed for the treatment of hyponatraemia associated with SIADH and is a vasopressin receptor antagonist. Initial dose is usually 15 mg daily and doses can be titrated depending on response to treatment.

Further Rrading:

Medscape tolvaptan (Rx)Samsca. Dosing and uses

Question 60

You are called to see a 42 year old female who has become particularly confused. She was admitted three days prior following an accident on her bike and had sustained a cerebral contusion. This did not require any neurosurgical intervention. On examination, she was drowsy with a Glasgow coma score of 13 and bilateral upgoing plantars but no focal neurology. Her pulse is 68 bpm with a blood pressure of 128/80 mmHg. Oxygen saturations are 99% on air.

Her blood results reveal the following:

		Normal Ranges
Sodium	118 mmol/l	(134-144)
Potassium	3.8 mmol/l	(3.5-5.5)
Urea	4.5 mmol/l	(3-8)
Creatinine	80 micromol/l	(50-100)
Glucose	4.8 mmol/l	(3.5-5.5)

Which of the following would be the most appropriate initial treatment for this patient?

- **A)** 100 mg IV hydrocortisone stat
- **B)** 150 mls of 3% hypertonic saline given over 20 mins
- **C)** 1 g phenytoin IV over 30 mins
- **D)** 1 l N saline over 4 hrs
- **E)** Fluid restriction to 500 mls per day

Answer

Correct answer : 150 mls of 3% hypertonic saline given over 20 mins

This patient appears to have developed a hyponatraemic encephalopathy associated with the severe and acute hyponatraemia. This seems likely due to either SIADH or indeed cerebral salt wasting. In this scenario, the acute development of hyponatraemia results in cerebral oedema associated with an osmotic influx of water into the brain cells and swamping of the counterregulatory sodium-potassium pump. The resulting cerebral oedema is life threatening and manifests as headache, drowsiness, seizure and potentially death. Therefore, urgent treatment is required and guidance recommends rapid increase in sodium by approx 5 mmol/l through use of 150 ml boluses of 3% hypertonic saline.M

Steroids will not help in this scenario despite the cerebral oedema. The patient does not have hypoadrenalism as reflected by normal potassium and blood pressure.

Reference

- Goce Spasovski et al (2014) European Society of Endocrinology Clinical Practice Guidelines on diagnosis and treatment of hyponatraemia

Question 61

You are called to see a 42 year old male patient on the neurosurgical ward. He was admitted with a head injury 3 days ago which required only observation. However, he has become more confused in the last 12 hours and his most recent U+Es performed this morning reveal:

		Normal Ranges
Sodium	125 mmol/l	(134-144)
Potassium	4.5 mmol/l	(3.5-5.5)
Urea	6.8 mmol/l	(3-8)
Urine Osmolality	620 mosmol/l	
Urine Sodium	125 mmol/l	

Checking through his records, the previous days his U+Es were normal. He had been allowed to eat and drink normally and had stopped IV fluids 2 days ago. He was on dexamethasone the dose of which had been reduced to 4 mg daily from 8 mg daily over the last day but he was on no other treatment.
On examination, he had Glasgow coma scale of 15, though seemed confused with him being disorientated. Oxygen saturations were 97% on air and his blood pressure was 110/80 mmHg with a pulse of 88 bpm.
Which of the following is the most likely diagnosis?

- **A)** Acute hypoadrenalism
- **B)** Cerebral salt wasting
- **C)** Pituitary apoplexy
- **D)** Syndrome of inappropriate ADH secretion
- **E)** Type IV renal tubular acidosis

Answer

Correct answer : Cerebral salt wasting

The most likely diagnosis in this patient with head injury who then develops acute symptomatic hyponatraemia and grossly elevated urine sodium is cerebral salt wasting (CSW). The grossly elevated urine sodium (>100) is highly suggestive as the sodium is usually less with SIADH. Similarly with SIADH, there is a dilutional element so urea and potassium typically reflect this dilution being themselves low normal in contrast to CSW where there is hypovolaemia and hence higher concentrations. Hypoadrenalism is an incorrect answer as the patient is already on a high dose of steroids – dexamethasone 4 mg/d.

References

- Cerebral Salt Wasting Medscape

Question 62

An 18 year old female is admitted as an emergency with acute facial swelling and difficulty breathing. She is not known to have any allergy but does suffer from mild asthma for which she occasionally uses a salbutamol inhaler. She was out having a picnic with her friends, eating various foods, when she suddenly became unwell, feeling particularly anxious and itchy, while developing facial/mouth swelling with difficulty breathing. Her friends called 999.
On examination, she has swelling of the face particularly around the eyes and lips. There are wheals around the neck. Pulse is 100 bpm and blood pressure 128/80 mmHg. She has an audible wheeze and oxygen saturations are 96% on air.
Which of the following is the most appropriate treatment for this patient?

- **A)** 0.5 mg adrenaline IV
- **B)** 0.5 mg adrenaline IM
- **C)** 10mg chlorpheniramine IM
- **D)** 100mg hydrocortisone IV
- **E)** 40mg oral prednisolone

Answer

Correct answer : 0.5 mg adrenaline IM

This patient has developed angioedema, urticarial and breathing difficulties typical of anaphylaxis. The patient should be treated with 0.5 mg IM adrenaline as the initial treatment as per the resuscitation council guidelines. Other treatments include IM/IV hydrocortisone and IM chlorpheniramine but the IM adrenaline and fluids is the initial treatment. The use of IV adrenaline is reserved for severe cases in whom expert understanding of IV adrenaline is understood.

Reference

- Resuscitation Council Guidelines on Anaphylaxis

Question 63

An 18 year old student is admitted after having had a strange reaction where she became acutely unwell after going to a Chinese restaurant. She became light headed and short of breath and she thinks she momentarily passed out. An ambulance was called and she was given oxygen and recovered. She has a history of eczema but nothing else. On examination, there is nothing to find and she seems fine. Blood results are normal.
Which of the following tests could be used to assess if this were an anaphylactic reaction?

- **A)** Alpha-1 antitrypsin
- **B)** C1-esterase
- **C)** C4 complement
- **D)** C-reactive protein
- **E)** Mast cell tryptase

Answer

Correct answer : Mast cell tryptase

Mast cell tryptase is the molecule to measure in suspected anaphylaxis as the mast cells release this in abundance in anaphylaxis with concentrations rising abruptly within 30 minutes to 1 hour. C1 esterase deficiency is a cause of repeated episodes of anaphylaxis but this is not the molecule to measure. As in this case, the measurement of mast cell tryptase may differentiate between a faint and anaphylaxis where doubt exists.

Reference:

- Resuscitation Council Guidelines anaphylaxis

Question 64

A 72 year old man with a 12 year history of diabetes being treated with metformin is seen as he is lethargic and the GP is concerned about his persistent hyperkalaemia. His 58.5 mmol/mol (7.5%) (< 53 mmol/mol (7)). He also has a history of hypertension for which he takes bisoprolol 5 mg daily, amlodipine 10 mg/d, simvastatin 40 mg/d and aspirin 75 mg/d.
He has been re-referred to clinic by his GP as he has been noted to have a persistent hyperkalaemia. Previously he was taking an ACE inhibitor but this was stopped one year ago.

		Normal Ranges
Sodium	132 mmol/l (134-144)	
Potassium	5.8 mmol/l	(3.5 – 5)
Urea	8.8 mmol/l	(3-8)
Creatinine	100 micromol/l	(50-100)
Glucose	14.1 mmol/l	(3.5-5.5)

Which of the following is the likely cause of this man’s hyperkalaemia?

- **A)** Autoimmune hypoadrenalism
- **B)** Bisoprolol
- **C)** Chronic renal failure
- **D)** Metformin
- **E)** Renal artery stenosis

Answer

Correct answer : Bisoprolol

This patient has a long history of hypertension and hyperkalaemia. He has a mild hyponatraemia associated with the hyperkalaemia and the most likely diagnosis is type 4 renal tubular acidosis or hyporeninaemic hypoaldosteronism. The most likely drug to cause this is the beta blocker and this should be stopped. Other drugs implicated include ACE inhibitors and NSAIDs.

Reference:

- Hyporeninaemic hypoaldosteronism

Question 65

A 45 year old female presents with a 3 month history of sweats and diarrhoea. She has watery diarrhoea 5-6 times daily and is also aware of flushes which occur daily without any obvious precipitant. She feels these symptoms have become more obvious and have been associated with some weight loss of 2 kg over the last 3 months. There is no past history of note and she takes no medication. There is nothing to note on examination with a BMI of 24.5 kg/m^2. Stool culture is negative. FBC, electrolytes, LFTs, calcium and thyroid function are all normal. A CT scan of the abdomen reveals numerous small metastatic deposits in the liver and some thickening around the appendix/ileocecal junction.

Which of the following tumour markers would be most helpful in this patient?

- **A)** CA 19-9
- **B)** CA 125
- **C)** CEA
- **D)** Chromogranin A and B
- **E)** HCG

Answer

Correct answer : Chromogranin A and B

This patient presents with a classical history of flushes and diarrhoea together with metastatic deposits in the liver suggesting metastatic neuroendocrine tumour (carcinoid syndrome). Useful tumour markers in this condition include chromogranin A and B and urinary 5-HIAA with 85% sensitivity and 95% sensitivity.

- Chromogranin A: Is it a useful tumour marker in NETs

Question 66

A 45 year old woman is diagnosed with acromegaly. Her IGF-1 concentration is elevated at 110 nmol/l (14-30) and she fails to suppress growth hormone concentrations on an oral glucose tolerance test. MRI of the pituitary confirms a pituitary macroadenoma which is distinct from the optic chiasm.

She is acromegalic in appearance, has a blood pressure of 140/80 mmHg. There is nothing else of note on examination and visual fields are full.

All other tests including FBC, U+Es, LFTs and TFTs are normal.

She is to have pituitary surgery in due course.

Which of the following investigations of the GI tract should also be undertaken on this patient?

- **A)** Chromogranin A and B
- **B)** Colonoscopy
- **C)** CT scan of abdomen
- **D)** Endoscopy
- **E)** Fasting gut peptides

Answer

Correct answer : Colonoscopy

This woman with active acromegaly should have a colonoscopy according to guidance. Individuals over the age of 40 with acromegaly should be screened with further interval screening performed at 3 years for those not cured or with polyps present.

Screening guidelines for acromegaly

Question 67

A 55 year old man is diagnosed with metastatic small bowel neuroendocrine tumour. He is noted to have a reddened scaly rash around his neck in a necklace-like effect. Which of the following is likely to be responsible for this rash?

- **A)** Niacin deficiency
- **B)** Pyridoxine deficiency
- **C)** Riboflavin deficiency
- **D)** Selenium deficiency
- **E)** Vitamin C deficiency

Answer

Correct answer : Niacin deficiency

Carcinoid syndrome is associated with the pellagra as the tumour elaborates serotonin from tryptophan, a component of niacin (vitamin B3).

- DermnetNZ Pellagra

Question 68

A 45-year-old engineer was referred by his GP with confusion, sweating and shaking mainly in the early morning. His symptoms were relieved on eating food. He was having 3 to 4 episodes of these symptoms a day. He had no significant past medical history. He was not on any medication. He had no family history of endocrinopathy, in particular there are no problems with the parathyroid, pituitary or pancreas. On examination, he had central obesity. Otherwise his general and systemic examination were unremarkable. His venous blood sugars when he had symptoms were 2.4 mmol/L, 2.6 mmol/L and 2.8 mmol/L respectively. He underwent a 72 hour fast and the results showed the following at 20 hrs into the fast:

		Normal Ranges
Insulin	30 mU/L	(10-50)
C-peptide	499 pmol/l	(94-300)
Corresponding glucose	2.3mmol/l	

His urine sulphonylurea screen is negative
He underwent a CT scan, MRI and endoscopic ultrasound and all were reported normal. What is the most appropriate next step?

- **A)** Lifelong diazoxide
- **B)** Lifelong prednisolone
- **C)** MR angiography
- **D)** PET scan of pancreas
- **E)** Selective intra-arterial calcium stimulation angiography

Answer

Correct answer : Selective intra-arterial calcium stimulation angiography

Explanation:

The above patient had spontaneous hypoglycaemia with inappropriately high insulin and C peptide levels suggestive of insulinoma. The mean diameter of insulinomas is generally not more than 15 mm and non-invasive imaging modalities often fail to localise them. Selective intra-arterial calcium stimulation with hepatic venous sampling is a highly accurate and safe method for the preoperative localization of insulinomas. A twofold rise in insulin levels following calcium gluconate injection of the gastroduodenal artery or superior mesenteric artery would indicate that the tumour is located in the pancreatic head or uncinate process; a twofold rise after injection into the splenic artery would suggest a corporeal or caudal location.

Sung, Y.M., Do, Y.S., Lee, M.K., Shin, S.W., Liu, W.C., Choo, S.W. and Choo, I.W., 2003. Selective intra-arterial calcium stimulation with hepatic venous sampling for preoperative localization of insulinomas. Korean journal of radiology, 4(2), pp.101-108.

Question 69

A 25-year-old man of Mediterranean origin presented to the accident and emergency department with a chest infection. He had no significant past medical history or family history. He was prescribed cotrimoxazole for his chest infection. On the third day, his chest infection improved but he developed a haemolytic anaemia. Further investigations revealed that he had glucose 6-phosphate dehydrogenase (G6PD) deficiency. What is the mode of inheritance of this condition?

- **A)** Autosomal dominant
- **B)** Autosomal recessive
- **C)** Mitochondrial inheritance
- **D)** Polygenic
- **E)** X linked recessive

Answer

Correct answer : X linked recessive

Explanation:

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the most common enzymatic disorder of red blood cells. It is inherited as X linked recessive pattern. The majority of the affected individuals are asymptomatic. Acute haemolytic anaemia typically develops within 24 to 72 hours following exposure to oxidative stress such as infections, drugs and ingestion of fava beans etc. Haemolysis is usually self-limited and resolves in 8 to 14 days.

Question 70

A 50-year-old female is referred with a 3-month history of tiredness and fatigue. Her GP had checked some bloods and found that she was euthyroid but had a triglyceride of 11.1 mmol/l (<2.5), a cholesterol of 7 mmol/l (3.5-5.5) and glucose of 5.3 mmol/l. She has a history of hypertension for which she takes Lisinopril 20mg daily and bendrofluazide 2.5 mg daily. She also takes omeprazole 20mg daily for GORD.

She has a strong family history of coronary artery disease with her father having died of a MI at 45, although he was a smoker and her paternal uncle having had coronary artery bypass before the age of 50.

On examination, she has a BMI of 29.3kg/m^2, appears clinically euthyroid, and there are no xanthomas/xanthelasma. Blood pressure was 132/80mmhg and nothing else was to be found on examination.

Fasting bloods revealed:

Test	Result	Normal Range
Triglycerides	6.5 mmol/l	
Cholesterol	7.1 mmol/l	
Glucose	4.2 mmol/l	
LFTs	Normal	
T4	9.3 nmol/l	(9-21)
TSH	2.1 mu/l	(0.5-4.5)

Which of the following would be the most appropriate treatment for this patient?

- **A)** Lifestyle interventions and add a fibrate
- **B)** Lifestyle interventions and add a statin
- **C)** Lifestyle interventions and add omega-3 free fatty acids
- **D)** Lifestyle interventions and add thyroxine
- **E)** Lifestyle interventions, stop bendrofluazide and add a statin

Answer

Correct answer : Lifestyle interventions, stop bendrofluazide and add a statin

Explanation:

This patient's family history is more in keeping with familial hypercholesterolaemia than combined hyperlipidaemia as her paternal side of the family presents with premature coronary artery disease. On this basis calculating this patient's risk based on QRISK3 criteria, she has an approximate 10% chance of a CV event in the next 10 yrs. Consequently, the patient should receive advice on lifestyle interventions and should also be treated with a statin due to her combined hyperlipidaemia. Drug-induced causes of hyperlipidaemia should also be considered and, in this case, the thiazide diuretic may contribute to the hypertriglyceridaemia and should be stopped.

Reference:

- NHS Guidance on treating hypertriglyceridaemia

Question 71

The FOURIER study published in the NEJM (2017), compared the addition of the PCSK-9 inhibitor, Evolucamab plus standard cholesterol reduction therapy versus standard cholesterol reduction therapy alone in 27000 patients with cardiovascular disease. The study was undertaken over 48 weeks.

What was the impact on LDL-cholesterol of the addition of evolucamab?

- **A)** 10% reduction
- **B)** 25% reduction
- **C)** 40% reduction
- **D)** 50% reduction
- **E)** 60% reduction

Answer

Correct answer : 60% reduction

Explanation:

Evolucamab in the FOURIER study resulted in an absolute reduction in cholesterol in individuals at high risk of cardiovascular disease from 1.8 mmol/l in those on standard therapy (statins etc) to 0.78 mmol/l; an approximate 1 mmo/l reduction (59%) reduction in cholesterol. PCSK-9 inhibitors (evolucamab and alirocumab) act via PCSK-9 inhibition. PCSK-9 is a molecule that binds to the LDL-C receptor speeding up its internalisation. Therefore inhibition of this molecule results in longer expression of the LDL-C receptor so enabling greater binding with LDL-C and large reductions in cholesterol concentrations.

Reference:

- FOURIER Steering Committee and Investigators, ‘Evolocumab and Clinical Outcomes in Patients with Cardiovascular Disease, The New England Journal of Medicine [May 2017]

Question 72

The FOURIER study published in the NEJM (2017), compared the addition of the PCSK-9 inhibitor, Evolucmab plus standard cholesterol reduction therapy with standard cholesterol reduction alone in 27000 patients with cardiovascular disease. The study was undertaken over 48 weeks. What was the impact of the addition of evolucamab upon the primary composite end point of cardiovascular mortality at the end of the study?

- **A)** No differences in relative or absolute risk reduction between the groups
- **B)** 5% non-significant relative risk reduction in CV mortality
- **C)** 15% significant relative risk reduction in CV mortality
- **D)** 30% relative risk reduction in CV mortality
- **E)** 40% relative risk reduction in CV mortality

Answer

Correct answer : 15% significant relative risk reduction in CV mortality

Explanation:

PCSK-9 inhibitors (evolucamab and alirocumab) function via preventing the internalisation of the LDL-C receptor so enabling large reductions in cholesterol concentrations. Evolucamab in the FOURIER study resulted in the reduction in a reduction in cholesterol in individuals at high risk of cardiovascular disease from 1.8 mmol/l in those on standard therapy (statins etc) to 0.78 mmol/l; a 59% reduction in cholesterol. At the end of the study at 48 weeks, this reduction in LDL-C was associated with an approximate 2% reduction in absolute CV mortality (15% relative risk reduction) as the primary end point as well as a 20% relative risk reduction in non-fatal secondary CV end points.

Reference:

- FOURIER Steering Committee and Investigators, ‘Evolocumab and Clinical Outcomes in Patients with Cardiovascular Disease, The New England Journal of Medicine [May 2017]

Question 73

The ODYSSEY outcomes trial (NEJM 2018) randomised nearly 19000 individuals who had proceeding acute coronary syndrome (1-12 months prior) to the PCSK-9 inhibitor, Alirocumab, or placebo together with standard statin/antiplatelet therapy. The study ran for 2.8 years. What effect did intervention have on the primary outcome measure measure of major adverse cardiovascular events (MACE)?

- **A)** A 2% significant absolute increase in MACE
- **B)** A significant 2% absolute reduction in MACE in the alirocumab group
- **C)** A significant 5% absolute reduction in MACE in the alirocumab group
- **D)** A significant 10% absolute reduction in MACE in the alirocumab group
- **E)** Non-inferiority in MACE between the two groups

Answer

Correct answer : A significant 2% absolute reduction in MACE in the alirocumab group

Explanation:

The ODYSSEY Outcome trial, a secondary prevention study of the PCSK-9 inhibitor, Alirocumab, revealed an approximate 1.3 mmol/l (50%) reduction in LDL-C (101 mg/dl vs 53 mg/dl) between groups and was associated with a 2% absolute risk reduction in MACE (15% relative risk reduction) and a 1.6% absolute risk reduction (20% relative risk reduction) in secondary end points (death/MI/Stroke). The suggestion is that PCSK-9 inhibitors may offer an added therapy with failure to achieve adequate target LDL-cholesterol with conventional cholesterol reduction using statins/ezetimibe etc (2 mmol/l 78 mg/dl).

Reference:

- ODYSSEY OUTCOMES Committees and Investigators, ‘Alirocumab and Cardiovascular Outcomes after Acute Coronary Syndrome’, The New England Journal of Medicine [November 2018]

Question 74

In the SCALE obesity and prediabetes study published in the NEJM (2015) which looked at the effects of 3 mg of Liraglutide as part of a placebo control study, what impact did treatment with Liraglutide have on the primary outcome measure of weight loss over this one year study?

- **A)** Treatment had no significant effect on weight loss
- **B)** Treatment was associated with a significant mean 3kg weight loss
- **C)** Treatment was associated with a significant 5kg weight loss
- **D)** Treatment was associated with a significant 8kg weight loss
- **E)** Treatment was associated with a significant 12kg weight loss

Answer

Correct answer : Treatment was associated with a significant 8kg weight loss

Explanation:

The landmark SCALE study compared the use of 3 mg daily liraglutide in 3000 obese or prediabetic patients plus lifestyle interventions with lifestyle alone. Liraglutide was associated with a significant 8kg weight loss (8% vs 2.6% loss) at the end of the 52 week study. These are particularly promising data supporting the role of GLP-1 analogues in obesity management.

Reference:

- SCALE Obesity and Prediabetes NN8022-1839 Study Group, 'A Randomized Controlled Trial of 3 mg of Liraglutide in Weight Management', The New England Journal of Medicine. [July 2015].

Question 75

Through which of the following mechanisms does Lorcaserin work as an anti-obesity agent?

- **A)** Noradrenergic reuptake inhibitor
- **B)** Opioid receptor Mu2 receptor antagonist
- **C)** PYY 3-36 selective receptor inhibitor
- **D)** Serotonin 2C receptor agonist
- **E)** Serotonin reuptake inhibitor

Answer

Correct answer : Serotonin 2C receptor agonist

Explanation:

Lorcaserin is a serotonin 2C receptor agonist which is associated with significant weight loss in placebo controlled studies. A more recent study revealed that vs lifestyle interventions it was associated with a 10% weight loss in close to 40% of subjects versus 17% in the placebo group.

Reference:

- CAMELLIA-TIMI 61 Steering Committee and Investigations, ‘Cardiovascular Safety of Lorcaserin in Overweight or Obese Patients, The New England Journal of Medicine; [September 2018].

Question 76

A 2018 publication in the NEJM compared the impact of the weight loss agent Lorcaserin on the cardiovascular risk in a high risk population versus placebo. In comparison to placebo arm, Lorcaserin was associated with significant weight loss but what impact did the drug have on cardiovascular risk?

- **A)** Lorcaserin showed no significant difference in cardiovascular risk
- **B)** Lorcaserin was associated with a 10% relative increase in cardiovascular risk
- **C)** Lorcaserin was associated with a significant 20% relative increase in cardiovascular risk
- **D)** Lorcaserin was associated with a significant 25% relative decrease in cardiovascular risk
- **E)** Lorcaserin was associated with a significant 30% relative increase in cardiovascular risk

Answer

Correct answer : Lorcaserin showed no significant difference in cardiovascular risk

Explanation:

In this landmark publication, Lorcaserin was found to have non-inferiority in cardiovascular end points versus placebo providing valuable supportive data for the safety of this drug in the treatment of obesity. Other agents such as sibutramine, phentermine etc with similar modes of action have had be withdrawn due to increased cardiovascular risk.

Reference:

- CAMELLIA-TIMI 61 Steering Committee and Investigations, ‘Cardiovascular Safety of Lorcaserin in Overweight or Obese Patients, The New England Journal of Medicine; [September 2018].

Question 77

The landmark publication, IMPROVE-IT in the NEJM (2015) compared the addition of ezetimibe 10mg daily on cardiovascular risk in individuals being treated with traditional lipid lowering therapy (Simvastatin) over 7 years. There was a significant 0.4 mmol/l reduction in the LDL-cholesterol in the ezetimibe-simvastatin group vs the simvastatin group. Compared with simvastatin only, what was the impact of this on the composite primary end point of cardiovascular risk?

- **A)** Non inferiority of ezetimibe-simvastatin on CV risk
- **B)** Significant 2% absolute risk reduction in CV risk
- **C)** Significant 3% increased CV risk associated with the simvastatin- ezetimibe treatment
- **D)** Significant 5% absolute risk reduction in CV risk
- **E)** Significant 8% absolute risk reduction in CV risk

Answer

Correct answer : Significant 2% absolute risk reduction in CV risk

Explanation:

The IMPROVE-IT study confirmed that LDL-cholesterol reduction is the most important factor in reducing CV risk rather than this being one of the pleiotropic effects of statins. Some experts suggested that the reductions in CV risk with previous statin studies such as 4S, CARE, WOSCOPS, HPS were a specific consequence of statins rather than LDL-C reduction. IMPROVE-IT supports the LDL-C reduction hypothesis as the reduction in risk is consistent with what one expects from LDL-C reduction. Associated with this small reduction in LDL-C there was a small but significant 2% absolute risk reduction in CV risk (relative risk reduction roughly 10%).

Reference:

- IMPROVE-IT Investigators, ‘Ezetimibe Added to Statin Therapy after Acute Coronary Syndromes, The New England Journal of Medicine. [June 2015]

Question 78

A 31-year-old woman presented to medical emergency admissions with a week history of dizziness and weakness together with a 2 day history of vomiting and diarrhoea. In her past medical history she was diagnosed with hypothyroidism 3 years ago and has been taking a stable dose of thyroxine 100 micrograms daily.

On examination, she seemed unwell and dehydrated, had a temperature of 37°C, pulse of 105 bpm a blood pressure of 94/68 mmHg and a BMI of 21. There was diffuse abdominal tenderness without any focal signs. Bowel sounds were normal. Initial investigations revealed:

FBC	Normal
Sodium	121 mmol/l (134-144)
Potassium	3.5 mmol/l (3.5-5.0)
Urea	8.8 mmol/l (3-8)
Creatinine	150 µmol/l (50-100)
Glucose	3.3 mmol/l (3.5-5.5)
CRP	55 mg/l (<5)

Which of the following is the most appropriate approach to the management of this patient?

- **A)** Administer IV bolus of hypertonic saline with IM cyclizine
- **B)** Administer IV 10% dextrose infusion, IM cyclizine and IV broad spectrum antibiotics
- **C)** Administer IV 10% dextrose with IV normal saline and IV broad spectrum antibiotics
- **D)** Administer IV hydrocortisone and IV normal saline
- **E)** Administer IV normal saline, IM cyclizine and IV broad spectrum antibiotics

Answer

Correct answer : Administer IV hydrocortisone and IV normal saline

Explanation

This patient has a prior autoimmune condition and presents with a seeming chronic hyponatraemia (acute hyponatraemia would more probably result in features of encephalopathy), lower normal potassium (vomiting and diarrhoea) together with tachycardia and hypotension. These features suggest an unrecognised adrenal crisis most likely due to associated Addison's disease and the patient requires urgent IV hydrocortisone and fluid resuscitation with normal saline at this point.

Explanation

- Daniel J. Toft, D.J., (2014) Addison's Disease Treatment Medications and How to Avoid an Addisonian Crisis. Endocrineweb

Question 79

A 60-year-old man is admitted with a 3 day history of deteriorating lethargy and confusion. The GP had undertaken bloods of which, the sodium was reported as 121 mmol/l (134-144).
Which of the following parameters would be most supportive of a diagnosis of SIADH?

- **A)** Plasma osmolality of 250 mOsm/kg
- **B)** Urinary sodium 12 mmol/l
- **C)** Urine osmolality of 350 mOsm/kg
- **D)** Presence of ankle oedema
- **E)** Potassium of 5.1 mmol/l (NR 3.5-5)

Answer

Correct answer : Urine osmolality of 350 mOsm/kg

Explanation

In the above, oedema would suggest a hypervolaemic hyponatraemia. SIADH is associated with a euvolaemic hyponatraemia with inappropriate concentration of the urine. Therefore, the inappropriately high urine osmolality would be in keeping with SIADH. A low urine sodium ie <20 mmol/l is suggestive of appropriate sodium retention and argues against a diagnosis of SIADH. Hyperkalaemia would suggest hypoadrenalism.

Question 80

A 33 year old female presents with a lump in the left side of the neck. Investigations confirm this to be a paraganglioma. With which of the following mutations are Paragangliomas associated?

- **A)** BRAF V600 mutatione
- **B)** MENIN mutation
- **C)** NF 2 mutation
- **D)** SDHB mutation
- **E)** VHL mutation

Answer

Correct answer : SDHB mutation

The 2004 WHO classification of endocrine tumours classifies catecholamine secreting tumours into intra-adrenal paragangliomas (classically known as phaeochromocytomas) and extra-adrenal paragangliomas. The latter are further subdivided into those arising from sympathetic tissue or parasympathetic tissues (usually located in head and neck, rarely produce catecholamine). Hereditary catecholamine producing intra or extra- adrenal paragangliomas can be caused by one of the following germ line mutations:

1. RET proto-oncogene
2. von Hippel-Lindau gene (vHL)
3. Neurofibromatosis Type 1 gene (NF-1)
4. Succinate dehydrogenase subunit B (SDHB)
5. Succinate dehydrogenase subunit D (SDHB)

Patients with SDHB or SDHD are more likely to present with extra-adrenal disease, bilateral tumours and metastatic disease. According to the guidelines issued by The First International Symposium on Phaeochromocytomas (October 2005), genetic screening should be individualised and is generally warranted in:

- Patients aged < 50 years, presenting with catecholamine secreting
- Multiple tumours
- Malignant tumours
- Bilateral tumours

Question 81

A 65 year old female with a 6 year history of breast cancer treated with mastectomy and receiving tamoxifen presents at clinic feeling tired and thirsty over the last few months. She has been under review for arm pain following surgery but surgery was successful and the oestrogen receptor positive tumour removed with no evidence of nodal spread. There are no specific abnormalities to find on examination but her blood results return as follows:

Calcium	3.1 mmol/l	(2.2-2.6)
Phosphate	0.8 mmol/l	(0.8 - 1.5)
Alkaline Phosphatase	145 mu/l	(50-110)
ESR	15 mm/hr	(0-10)
PTH	5 pmol/l	(3-5.5)

Which of the following is the most likely diagnosis?

- **A)** Ectopic PTH secretion
- **B)** Metastatic hypercalcaemia
- **C)** Primary hyperparathyroidism
- **D)** Secondary hyperparathyroidism
- **E)** Tumoral vitamin D secretion

Answer

Correct answer : Primary hyperparathyroidism

Good discriminatory question here and one often asked in exams.

This patient has hypercalcaemia with an inappropriately high-normal PTH. The diagnosis is therefore primary hyperparathyroidism. If this were tumoral related hypercalcaemia, then, through negative feedback, the PTH concentration should be suppressed. Ectopic PTH or tumoural PTH is not picked up in the traditional PTH assay and again, therefore if this were the cause the PTH would have to be lower. This patient has hypercalcaemia with an inappropriately high-normal PTH. The diagnosis is therefore primary hyperparathyroidism. If this were tumoral related hypercalcaemia, then, through negative feedback, the PTH concentration should be suppressed.

Question 82

A 66 year old female with a 2 year history of metastatic bowel carcinoma presents to emergency admissions with a 2 week history of gradual general deterioration.
On examination, she appears unwell and dehydrated with a blood pressure of 118/72 mmHg and a temperature of 37C. Her results reveal the following:

Sodium	144 mmol/l	(134 - 144)
Potassium	5 mmol/l	(3.5-5)
Urea	22.6 mmol/l	(3-8)
Creatinine	198 micromol/l	(50-100)
Calcium	4.0 mmol/l	(2.2-2.6)
Phosphate	0.8 mmol/l	(0.8 - 1.5)
Alkaline Phosphatase	845 mu/l	(50-110)
ESR	100 mm/hr	(0-10)

Which of the following is the most appropriate immediate treatment for this patient?

- **A)** IV normal saline
- **B)** IV Pamidronate
- **C)** IV Prednisolone
- **D)** IV Zolendronate
- **E)** Subcutaneous Calcitonin

Answer

Correct answer : IV normal saline

The most appropriate immediate treatment for this patient with severe hypercalcaemia, which is probably metastatic, would be IV resuscitation with normal saline ~200-300mls/hr. IV frusemide with a forced diuresis might also be considered. Addition of Calcitonin may also be useful acutely if the calcium remains stubbornly high. Once the patient has been adequately rehydrated, IV bisphosphonates would be appropriate in the first instance. Bisphosphonates usually take roughly 2-3 days to begin

https://www.uptodate.com/contents/treatment-of-hypercalcemia

Question 83

A 65 year old male is admitted feeling generally unwell having had problems with lethargy and thirst. He has been diagnosed with metastatic renal cell carcinoma for which he is treated with sunitinib. On examination, he appears dehydrated. His investigations reveal:

Haemoglobin	16.1 g/dl	(12-16)
White cell count	$5.5x10^9$/l	(3-10)
Platelets	310 $x10^6$/l	(150-400)
Sodium	136 mmo/l	(134-144)
Potassium	4.2 mmol/l	(3.5-5)
Urea	12.8 mmol/l	(3-8)
Creatinine	168 micromol/l	(50-100)
Calcium	3.2 mmol/l	(2.2-2.6)
Phosphate	0.8 mmol/l	(0.8-1.5)
PTH	1.0 pmol/l	(3-5.5)

Which of the following would you request to establish the likely cause of his presentation?

- **A)** 1,25 dihydroxy Vitamin D
- **B)** 25-Hydroxy Vitamin D
- **C)** Cortisol
- **D)** PTHrp
- **E)** Vitamin A

Answer

Correct answer : PTHrp

This patient presents with symptomatic hypercalcaemia which could be due to metastatic infiltration but also to ectopic elaboration of PTHrp by the renal cell carcinoma. The molecule behaves in a similar manner to PTH having close homology to the N-terminal sequence. Other tumours responsible for the elaboration of PTHrp include squamous cell carcinoma of the lung and breast carcinoma.

https://www.ncbi.nlm.nih.gov/pubmed/16223565

Question 84

A 60-year-old woman is admitted with a 2 hour history of chest pain. Her past medical history includes type 2 diabetes and hypertension. She was being treated with metformin 1 g bd, ramipril 5 mg daily and atorvastatin 10 mg daily. The patient is a non-smoker.

On examination, she has a BMI of 24 kg/m^2, a pulse of 110 bpm reg, a blood pressure of 160/100 mmHg, temperature 37°C and oxygen saturations of 95% on room air. No other abnormalities were present. BM glucose was 11.2 mmol/l without ketones. Troponin was 66 ng/l (<20).

Her ECG reveals anterior ST segment elevation and she undergoes coronary angiography. However, coronary angiography reveals normal coronary arteries. Echo showed left ventricular apical wall hypokinesis with an ejection fraction of 35-40%.

Which of the following is the most likely diagnosis?

- **A)** Coronary artery spasm
- **B)** Myocarditis
- **C)** Pulmonary embolism
- **D)** Takotsubo cardiomyopathy
- **E)** Type 2 myocardial infarction

Answer

Correct answer : Takotsubo cardiomyopathy

Explanation

This patient has indeed a type 2 MI as demonstrated by normal coronary arteries yet STEMI and a troponin rise. The patient has type 2 diabetes and hypertension but has a normal BMI. Similarly she has tachycardia and hypertension. The EF is impaired at <40%. This suggests a diagnosis of Takotsubo cardiomyopathy associated with a potential underlying diagnosis of phaeochromocytoma.

Takotsubo cardiomyopathy is also known as apical ballooning syndrome or broken heart syndrome. It is associated with phaeochromocytoma as well as occurring more commonly in postmenopausal females associated with severe anxiety/stress. It typically recovers within days or weeks.

Reference:

- American College of Cardiology. (n.d.). Diagnosing Type 2 Myocardial Infarction. [online] [Accessed 20 May 2020].

Question 85

A 16-year-old girl presented two years back with short stature. On evaluation she was found to have primary overt hypothyroidism secondary to autoimmune thyroiditis. She was started on levothyroxine (LT4). She was on a stable levothyroxine dose for a while which was recently increased on the account of having a higher TSH. After about a month, the patient presented to the emergency department with difficulty in breathing. The patient had been losing weight over the last few weeks which she wrongly attributed to the increase in the levothyroxine dose. She also had increased frequency of urination. On evaluation the patient was found to have diabetic ketoacidosis. She had GAD65 antibody positive and was labelled as having type 1 diabetes. She was also screened for celiac disease and adrenal insufficiency both of which were negative. What type of polyendocrine autoimmune syndrome (PAS) is the patient suffering from?

- **A)** Polyendocrine autoimmune syndrome (PAS) type 1
- **B)** Polyendocrine autoimmune syndrome (PAS) type 2
- **C)** Polyendocrine autoimmune syndrome (PAS) type 3
- **D)** Polyendocrine autoimmune syndrome (PAS) type 4
- **E)** She is not suffering from any polyendocrine autoimmune syndrome. The association of autoimmune thyroiditis and type 1 diabetes does not have a syndromic association

Answer

Correct answer : Polyendocrine autoimmune syndrome (PAS) type 3

Explanation:

Polyglandular autoimmune syndrome (PAS) also called autoimmune polyendocrine syndrome (APS) are a series of disorders characterised by immune mediated involvement of one or more endocrine organ (Valenzise et al., 2017).

Neufeld et al originally classified PAS into two distinct subtypes (NEUFELD, MACLAREN and BLIZZARD, 1981). PAS type 1, also called autoimmune polyendocrinopathy–candidiasis–ectodermal dystrophy (APECED) is a rare autosomal recessive pediatric endocrine disorder characterized by two or more of the following: chronic mucocutaneous candidiasis, hypoparathyroidism, and primary adrenal insufficiency. PAS type 2 consists of primary adrenal insufficiency with either type 1 diabetes or autoimmune thyroid dysfunction (NEUFELD, MACLAREN and BLIZZARD, 1981).

PAS type 3 was not a part of the original Neufeld and Blizzard classification of PAS but was added later. PAS type 3 is the most common form of autoimmune polyendocrine syndrome in both adults as well as in the pediatric age group. PAS type 3 is characterized by autoimmune thyroid disorder (ATD) associated with a second autoimmune disorder other than adrenal insufficiency. The association of ATD with type 1 diabetes is called PAS type 3a. A study showed that almost 30% of pediatric patients with ATD could be classified as having PAS type 3 (Valenzise et al., 2017). Autoimmune endocrine disorders not classified in PAS types 1 to 3 are classified as having PAS type 4 (Mihalache et al., 2016).

Reference:

- Mihalache, L. et al. (2016) 'A RARE CASE OF SEVERE TYPE 4 POLYGLANDULAR AUTOIMMUNE SYNDROME IN A YOUNG ADULT', Acta endocrinologica (Bucharest, Romania?: 2005). Acta Endocrinologica Foundation, 12(1), pp. 104–110. doi: 10.4183/aeb.2016.104.
- NEUFELD, M., MACLAREN, N. K. and BLIZZARD, R. M. (1981) 'Two Types of Autoimmune Addison's Disease Associated with Different Polyglandular Autoimmune (PGA) Syndromes', Medicine, 60(5)
- Valenzise, M. et al. (2017) 'Epidemiological and clinical peculiarities of polyglandular syndrome type 3 in pediatric age', Italian journal of pediatrics. BioMed Central, 43(1), p. 69. doi: 10.1186/s13052-017-0386-4.

Question 86

A 45-year-old woman is a known case of End-stage renal disease (ESRD) on maintenance dialysis awaiting renal transplant. Recently her nephrologist changed her anti-hypertensive medications. She is currently on alpha-methyldopa, prazosin and nifedipine for her blood pressure, apart from other medications. Of these, alpha-methyldopa and prazosin were recently introduced. After the change of the medication the patient started experiencing galactorrhea. The physician measured her prolactin which was 12,021 mIU/l (565 ng/ml, normal range <600 mIU/l). An MRI was done which showed no obvious pituitary lesion. Her thyroid function test is normal. The patient is not taking any other medication that can impact the dopaminergic system. What should be done next for this patient ?

- **A)** Change the alpha-methyl-dopa to some other anti-hypertensive medication
- **B)** Consider hemodialysis since dialysis can reduce the prolactin levels
- **C)** Since prolactin is elevated in ESRD patients, nothing needs to be done expect close observation
- **D)** Start the patient on bromocriptine for the galactorrhea and elevated prolactin
- **E)** Start the patient on cabergoline for the galactorrhea and elevated prolactin

Answer

Correct answer : Change the alpha-methyl-dopa to some other anti-hypertensive medication

Explanation:

Prolactin levels are elevated in patients with end-stage renal disease (ESRD). This is only partly due to reduced renal clearance. It is postulated that uremic toxins can impact the dopaminergic system leading to the reduced inhibition of prolactin secretion. The mean prolactin levels in patients with ESRD is 1382 mIU/l (65 ng/dl). In most patients with ESRD the prolactin levels are <2000 mIU/ml (100 ng/ml). In patients having higher prolactin levels, as seen in this case, an etiological evaluation to find the possible cause for the elevated prolactin including performing an MRI is necessary. (Williams et al., 2013)

Drugs and clinical conditions that lead to hyperprolactinemia in asymptomatic individuals can also cause worsening of the prolactin levels in patients with ESRD. The magnitude of the prolactin increase may also be higher. Alpha-methyldopa is well known to increase prolactin levels (Steiner et al., 1976) In this patient it is likely that the introduction of this medication led to an increase of prolactin making the patient symptomatic. Hence the best management for this patient would be to change the anti-hypertensive medication.(Pratap et al., 2008)

Though the use of bromocriptine can help reduce the prolactin levels, including in patients having ESRD, in this case stopping the offending medication would be a better solution. There is limited literature on the use of cabergoline in ESRD.

Hemodialysis does not significantly reduce the prolactin level in these patients. Renal transplant is helpful and helps to normalize the prolactin.(Pratap et al., 2008) Since the patient is symptomatic and we do know an offending agent, just close observation may not be the right approach.

Reference:

- Pratap, B. et al. (2008) ‘Cessation of galactorrhea in a chronic kidney disease patient with non-tumoral hyperprolactinemia after renal transplantation’, JOURNAL-ASSOCIATION OF PHYSICIANS OF INDIA. ASSOC OF PHYSICIANS OF INDIA, 56(N), p. 54.
- Steiner, J. et al. (1976) ‘Effects of methyldopa on prolactin and growth hormone.’, Br Med J. British Medical Journal Publishing Group, 1(6019), pp. 1186–1188.
- Williams, G. et al. (2013) ‘Chronic kidney disease: an uncommon cause of galactorrhoea in an adolescent’, in 41st Meeting of the British Society for Paediatric Endocrinology and Diabetes. BioScientifica.

Question 87

A 35-year-old man of Afro-Caribbean ethnicity presents with a 3-4 week history of deteriorating thirst, fatigue and polyuria. There is nothing else of note in his history. On examination, he appears dehydrated, his BMI is 33kg/m^2, pulse 100 bpm, temp 37^{o}C and blood pressure 122/80mmHg. His random plasma glucose was 27.3 mmol/l with ketones of 4.5 mmol/L (NR <0.6). His venous blood pH is 7.2 with a bicarbonate of 14 mmol/l. He is treated with IV fluids plus a fixed rate intravenous insulin infusion (FRIII).

Which of the following is the likely diagnosis and the most appropriate approach to his further management?

- **A)** He is likely to have type 1 diabetes and will require long-term insulin treatment
- **B)** He is likely to have type 2 diabetes. FRIII should be stopped and metformin commenced
- **C)** He is likely to have type 2 diabetes but will require long-term insulin
- **D)** The classification of his diabetes is unclear; FRIII should be continued until DKA improved and his subsequent glycaemia carefully assessed
- **E)** The classification of his diabetes is unclear; FRIII should be stopped and a sulphonylurea commenced

Answer

Correct answer : The classification of his diabetes is unclear; FRIII should be continued until DKA improved and his subsequent glycaemia carefully assessed

Explanation:

This patient presents an interesting case, presenting with DKA after a month-long illness in an Afro-Caribbean obese male. This could be type 1 diabetes or type 2 diabetes susceptible to DKA, so-called type 1.5 diabetes. Afro-Caribbean patients are particularly susceptible to this form of diabetes and the patient should be treated with the FRII to control the DKA then assessed thereafter. If type 2 diabetes he may not need insulin treatment long term and could be managed with oral agents.

Reference:

- GP Notebook - type 1.5 diabetes mellitus (flatbush diabetes)

Question 88

A 66-year-old male presented with a three-day history of fatigue and generalised pain. He was a type 2 diabetic with an HbA1c of 7% (53 mmol/mol) and was receiving metformin, ramipril and simvastatin. One month before admission, he underwent an endoscopy for dyspeptic symptoms which revealed H Pylori infection for which he was treated with clarithromycin, omeprazole and amoxicillin. He did not smoke but drank 15-20 units of alcohol weekly.

On examination, he appeared unwell with a temperature of 37.8^{o}C, a pulse of 110 bpm regular and a blood pressure of 136/88 mmHg. There was proximal muscle tenderness and weakness. Results revealed the following:

Test	Result	Normal Range
FBC	Normal	
Sodium	134 mmol/l	(134-144)
Potassium	4.6 mmol/l	(3.5-5.5)
Urea	12.8 mmol/l	(3-8)
Creatinine	162 micromol/l	(50-100)
Creatine Kinase	12,258 iu/l	(30-200)
AST	1500 iu/l	(<50)
ALT	2455 iu/l	(<50)

Which of the following is the likely precipitant of this man's rhabdomyolysis?

- **A)** Simvastatin – amoxicillin
- **B)** Simvastatin – clarithromycin
- **C)** Simvastatin – metformin
- **D)** Simvastatin – omeprazole
- **E)** Simvastatin – ramipril

Answer

Correct answer : Simvastatin – clarithromycin

Explanation:

This man presents acutely with rhabdomyolysis and this is likely to have been precipitated by the co-prescription of clarithromycin with simvastatin. Simvastatin is metabolised by cytochrome CYP3A4 which is inhibited by macrolides resulting in increased plasma concentrations of the statin and hence increased propensity to rhabdomyolysis. One should avoid the co-prescription of these agents and also other statins such as atorvastatin metabolised through this enzyme.

References:

- Lee, A.J. and Maddix, D.S., 2001. Rhabdomyolysis secondary to a drug interaction between simvastatin and clarithromycin. Annals of Pharmacotherapy, 35(1), pp.26-31.

Question 89

A 40-year-old male is admitted with a vague headache with a query of possible malignant hypertension after the GP had found the patient's blood pressure as 188/110 mmHg. He has morbid obesity and hyperlipidaemia for which he has been treated with liraglutide and atorvastatin 80mg daily together with ramipril. He is being considered for bariatric surgery as all therapeutic measures at weight loss have been unsuccessful. He has more recently been diagnosed with diabetes and has also commenced metformin 1g bd.

On examination, he has a weight of 160kg and a BMI of 52 kg/m^2. All observations are otherwise fine and there are no xanthomas/xanthelasmas to inspect. Fundal examination was normal and the blood pressure with an appropriately sized cuff was 136/90 mmHg.

Investigations reveal normal full blood count, U+Es and LFTs. Glucose is 10.2 mmol/l. His lipid profile is reported as lipaemia and reveals Cholesterol 10.6 mmol/l (<6) and Triglycerides 45.6 mmol/l (0.6 – 1.9). An ECG shows voltage criteria left ventricular hypertrophy. Amylase was 110 iu/l (30-110).

Which of the following is the most appropriate approach to the management of this patient?

- **A)** Add 3-omega fatty acid to his current medication and discharge
- **B)** Add a fibrate to his current medication and discharge
- **C)** Add nicotinic acid to his current medication and discharge
- **D)** Reassure and discharge. Continue on his current medication
- **E)** Start fixed rate insulin infusion

Answer

Correct answer : Start fixed rate insulin infusion

Explanation:

This patient does not have severe hypertension and it would seem that the earlier high blood pressure was due to an inadequately sized cuff. However, what has been revealed is a severe hypertriglyceridaemia. In this context, he is at risk of developing pancreatitis and acute coronary artery disease. A rapid reduction of hypertriglyceridaemia is required and this should be achieved through a fixed-rate insulin infusion rather than sliding scale insulin. Insulin is effective in the treatment of severe hypertriglyceridaemia as it promotes the action of lipoprotein lipase.

The onset of action of fibrates is too slow to be of use in this setting, nor are 3-omegaFFAs potent enough to bring about an adequate reduction with the targ triglyceride <10. The patient should also receive a low-calorie diet at this stage (800 – 1000 kcal/d) to facilitate a speedier reduction in triglycerides.

Aphaeresis has been advocated as a treatment for hypertriglyceridaemia in the context of pancreatitis. In this scenario, it is also important to determine the cause of the hypertriglyceridaemia. Often the cause is obscure, but hypothyroidism and alcohol excess contribute to type 2 diabetes and of course obesity itself.

Reference:

- Ewald, N. and Kloer, H.U., 2012. Treatment options for severe hypertriglyceridemia (SHTG): the role of apheresis. Clinical research in cardiology supplements, 7(1), pp.31-35.

Question 90

A 44 year old woman is admitted for further investigations of her hypoglycaemic episodes. Her 72 hour fasting blood results are shown below:

		Normal Ranges
Blood sugar	2.2 mmol/L	(3.5-5.5)
Insulin	155 µU/L	(<10)
C Peptide	10.2 pmol/L	(<500)
Sulfonylurea screen	negative	

What is the next best step to establish the likely underlying diagnosis?

- **A)** Check her IGF-1 to IGF-2 ratio
- **B)** CT abdomen
- **C)** CT angiography
- **D)** Enquire about likely use of exogenous injections
- **E)** Gut hormone profile

Answer

Correct answer : Enquire about likely use of exogenous injections

Hypoglycaemia in non-diabetics is traditionally classified as post-absorbtive (fasting) hypoglycaemia or postprandial (reactive) hypoglycaemia. However, whether a patient appears to be ill or well, is now regarded as a better factor in assessing the cause of hypoglycaemia. In a well appearing individual, causes of hypoglycaemia include:

- Drugs - insulin or insulin secretagogue; alcohol; other drugs
- Accidental, surreptitious, or malicious hypoglycaemia
- Endogenous hyperinsulinism - insulinoma; functional beta cell disorders nesidioblastosis); noninsulinoma pancreatogenous hypoglycaemia; post-gastric bypass hypoglycaemia; insulin autoimmune hypoglycaemia; anti-insulin antibody; anti-insulin receptor antibody
- Idiopathic postprandial hypoglycaemia

In this non-diabetic patient with hypoglycaemia, her fasting blood results reveal a raised insulin level with a normal c-peptide level, which is suggestive of an exogenous insulin source.

The biochemical pattern for different causes of hypoglycaemia in non-diabetics are as follows:

- Exogenous insulin - raised insulin, normal c-peptide, normal proinsulin, negative sulphonylurea, negative insulin antibody
- Insulinoma - raised insulin, raised c-peptide, raised proinsulin, negative sulphonylurea, negative insulin antibodies
- Sulphonylurea - raised insulin, raised c-peptide, raised proinsulin, positive sulphonylurea, negative insulin antibody

Reference:

- Hypoglycaemia in non-diabetic patients

Question 91

A 44 year old woman is admitted for further investigations of her hypoglycaemic episodes. Her 72 hour fasting blood results are shown below:

		Normal Ranges
Blood sugar	2.2 mmol/L	(3.5-5.5)
Insulin	155 µU/L	(<10)
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Answer

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- Insulinoma - raised insulin, raised c-peptide, raised proinsulin, negative sulphonylurea, negative insulin antibodies
- Sulphonylurea - raised insulin, raised c-peptide, raised proinsulin, positive sulphonylurea, negative insulin antibody

Reference:

- Hypoglycaemia in non-diabetic patients

Question 92

A 44 year old woman is admitted for further investigations of her hypoglycaemic episodes. Her 72 hour fasting blood results are shown below:

		Normal Ranges
Blood sugar	2.2 mmol/L	(3.5-5.5)
Insulin	155 µU/L	(<10)
C Peptide	10.2 pmol/L	(<500)
Sulfonylurea screen	negative	

What is the next best step to establish the likely underlying diagnosis?

- **A)** Check her IGF-1 to IGF-2 ratio
- **B)** CT abdomen
- **C)** CT angiography
- **D)** Enquire about likely use of exogenous injections
- **E)** Gut hormone profile

Answer

Correct answer : Enquire about likely use of exogenous injections

Hypoglycaemia in non-diabetics is traditionally classified as post-absorbtive (fasting) hypoglycaemia or postprandial (reactive) hypoglycaemia. However, whether a patient appears to be ill or well, is now regarded as a better factor in assessing the cause of hypoglycaemia. In a well appearing individual, causes of hypoglycaemia include:

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- Idiopathic postprandial hypoglycaemia

In this non-diabetic patient with hypoglycaemia, her fasting blood results reveal a raised insulin level with a normal c-peptide level, which is suggestive of an exogenous insulin source.

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- Insulinoma - raised insulin, raised c-peptide, raised proinsulin, negative sulphonylurea, negative insulin antibodies
- Sulphonylurea - raised insulin, raised c-peptide, raised proinsulin, positive sulphonylurea, negative insulin antibody

Reference:

- Hypoglycaemia in non-diabetic patients

Question 93

A 44 year old woman is admitted for further investigations of her hypoglycaemic episodes. Her 72 hour fasting blood results are shown below:

		Normal Ranges
Blood sugar	2.2 mmol/L	(3.5-5.5)
Insulin	155 µU/L	(<10)
C Peptide	10.2 pmol/L	(<500)
Sulfonylurea screen	negative	

What is the next best step to establish the likely underlying diagnosis?

- **A)** Check her IGF-1 to IGF-2 ratio
- **B)** CT abdomen
- **C)** CT angiography
- **D)** Enquire about likely use of exogenous injections
- **E)** Gut hormone profile

Answer

Correct answer : Enquire about likely use of exogenous injections

Hypoglycaemia in non-diabetics is traditionally classified as post-absorbtive (fasting) hypoglycaemia or postprandial (reactive) hypoglycaemia. However, whether a patient appears to be ill or well, is now regarded as a better factor in assessing the cause of hypoglycaemia. In a well appearing individual, causes of hypoglycaemia include:

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- Idiopathic postprandial hypoglycaemia

In this non-diabetic patient with hypoglycaemia, her fasting blood results reveal a raised insulin level with a normal c-peptide level, which is suggestive of an exogenous insulin source.

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- Insulinoma - raised insulin, raised c-peptide, raised proinsulin, negative sulphonylurea, negative insulin antibodies
- Sulphonylurea - raised insulin, raised c-peptide, raised proinsulin, positive sulphonylurea, negative insulin antibody

Reference:

- Hypoglycaemia in non-diabetic patients

Question 94

A 44 year old woman is admitted for further investigations of her hypoglycaemic episodes. Her 72 hour fasting blood results are shown below:

		Normal Ranges
Blood sugar	2.2 mmol/L	(3.5-5.5)
Insulin	155 µU/L	(<10)
C Peptide	10.2 pmol/L	(<500)
Sulfonylurea screen	negative	

What is the next best step to establish the likely underlying diagnosis?

- **A)** Check her IGF-1 to IGF-2 ratio
- **B)** CT abdomen
- **C)** CT angiography
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- **E)** Gut hormone profile

Answer

Correct answer : Enquire about likely use of exogenous injections

Hypoglycaemia in non-diabetics is traditionally classified as post-absorbtive (fasting) hypoglycaemia or postprandial (reactive) hypoglycaemia. However, whether a patient appears to be ill or well, is now regarded as a better factor in assessing the cause of hypoglycaemia. In a well appearing individual, causes of hypoglycaemia include:

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- Sulphonylurea - raised insulin, raised c-peptide, raised proinsulin, positive sulphonylurea, negative insulin antibody

Reference:

- Hypoglycaemia in non-diabetic patients

Question 95

A 44 year old woman is admitted for further investigations of her hypoglycaemic episodes. Her 72 hour fasting blood results are shown below:

		Normal Ranges
Blood sugar	2.2 mmol/L	(3.5-5.5)
Insulin	155 µU/L	(<10)
C Peptide	10.2 pmol/L	(<500)
Sulfonylurea screen	negative	

What is the next best step to establish the likely underlying diagnosis?

- **A)** Check her IGF-1 to IGF-2 ratio
- **B)** CT abdomen
- **C)** CT angiography
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Question 96

A 44 year old woman is admitted for further investigations of her hypoglycaemic episodes. Her 72 hour fasting blood results are shown below:

		Normal Ranges
Blood sugar	2.2 mmol/L	(3.5-5.5)
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- Hypoglycaemia in non-diabetic patients

Question 97

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- Hypoglycaemia in non-diabetic patients

Question 98

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		Normal Ranges
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- Hypoglycaemia in non-diabetic patients

Question 99

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		Normal Ranges
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Reference:

- Hypoglycaemia in non-diabetic patients

Question 100

A 44 year old woman is admitted for further investigations of her hypoglycaemic episodes. Her 72 hour fasting blood results are shown below:

		Normal Ranges
Blood sugar	2.2 mmol/L	(3.5-5.5)
Insulin	155 µU/L	(<10)
C Peptide	10.2 pmol/L	(<500)
Sulfonylurea screen	negative	

What is the next best step to establish the likely underlying diagnosis?

- **A)** Check her IGF-1 to IGF-2 ratio
- **B)** CT abdomen
- **C)** CT angiography
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Answer

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- Sulphonylurea - raised insulin, raised c-peptide, raised proinsulin, positive sulphonylurea, negative insulin antibody

Reference:

- Hypoglycaemia in non-diabetic patients

Question 101

A 44 year old woman is admitted for further investigations of her hypoglycaemic episodes. Her 72 hour fasting blood results are shown below:

		Normal Ranges
Blood sugar	2.2 mmol/L	(3.5-5.5)
Insulin	155 µU/L	(<10)
C Peptide	10.2 pmol/L	(<500)
Sulfonylurea screen	negative	

What is the next best step to establish the likely underlying diagnosis?

- **A)** Check her IGF-1 to IGF-2 ratio
- **B)** CT abdomen
- **C)** CT angiography
- **D)** Enquire about likely use of exogenous injections
- **E)** Gut hormone profile

Answer

Correct answer : Enquire about likely use of exogenous injections

Hypoglycaemia in non-diabetics is traditionally classified as post-absorbtive (fasting) hypoglycaemia or postprandial (reactive) hypoglycaemia. However, whether a patient appears to be ill or well, is now regarded as a better factor in assessing the cause of hypoglycaemia. In a well appearing individual, causes of hypoglycaemia include:

- Drugs - insulin or insulin secretagogue; alcohol; other drugs
- Accidental, surreptitious, or malicious hypoglycaemia
- Endogenous hyperinsulinism - insulinoma; functional beta cell disorders nesidioblastosis); noninsulinoma pancreatogenous hypoglycaemia; post-gastric bypass hypoglycaemia; insulin autoimmune hypoglycaemia; anti-insulin antibody; anti-insulin receptor antibody
- Idiopathic postprandial hypoglycaemia

In this non-diabetic patient with hypoglycaemia, her fasting blood results reveal a raised insulin level with a normal c-peptide level, which is suggestive of an exogenous insulin source.

The biochemical pattern for different causes of hypoglycaemia in non-diabetics are as follows:

- Exogenous insulin - raised insulin, normal c-peptide, normal proinsulin, negative sulphonylurea, negative insulin antibody
- Insulinoma - raised insulin, raised c-peptide, raised proinsulin, negative sulphonylurea, negative insulin antibodies
- Sulphonylurea - raised insulin, raised c-peptide, raised proinsulin, positive sulphonylurea, negative insulin antibody

Reference:

- Hypoglycaemia in non-diabetic patients

Question 1

A meta-analysis on pioglitazone reports an increased risk of fractures associated with the long term use of the drug. Which of the following effects of pioglitazone on bone is implicated in this increased fracture risk?

- **A)** Increased osteoclast activity
- **B)** Reduced osteoblast activity
- **C)** Reduced calcitonin secretion
- **D)** Reduced PTH secretion
- **E)** Reduced vitamin D synthesis

Answer

Correct answer : Reduced osteoblast activity

TZDs as a class have been associated with an increased risk of fracture. PPAR-gamma receptor activation in bone has been shown to reduce osteoblast activity, but have no effect on osteoclast activity resulting in an increase in fat deposition within bone. Pioglitazone is contraindicated in patients at risk of heart failure or with a previous history of heart failure. TZDs as a class have been shown to reduce bone specific alkaline phosphatase, but have no detrimental effects on left ventricular systolic function. Pioglitazone predominantly undergoes hepatic metabolism and are not recommended for patients with significant hepatic dysfunction, defined by transaminase levels 2.5 X the upper limit of normal.

Question 2

A 65 year old female is referred from primary care with various aches and pains. She has no past history of note and takes no medication. The GP encloses the following biochemistry:

		Normal Ranges
U+Es	Normal	
Calcium	2.36 mmol/l	(2.2 - 2.6)
Phosphate	0.8 mmol/l	(0.7 - 1.4)
PTH	18.2 nmol/l	(3 - 6)

Which of the following is the likely diagnosis?

- **A)** Familial hypercalciuric hypercalcaemia
- **B)** Primary hyperparathyroidism
- **C)** Pseudohypoparathyroidism
- **D)** Secondary hyperparathyroidism
- **E)** Tertiary hyperparathyroidism

Answer

Correct answer : Secondary hyperparathyroidism

This patient has a lowish calcium and elevated PTH concentration. The most likely explanation in a 65 year old female is vitamin D deficiency and hence secondary hyperparathyroidism. Vitamin D deficiency is common and some studies suggest that it is present to a variable extent in up to 30% of the general population.

Reference:

Emedicine Vitamin D deficiency

Question 3

A 65 year old female has been commenced on denosumab for the treatment of osteoporosis. Which of the following most appropriately describes the mechanism of action of denosumab?

- **A)** Increases bone remodelling
- **B)** Increases calcium reabsorption from the gut
- **C)** Inhibits osteoclast function
- **D)** Reduces osteoblast function
- **E)** Reduces renal calcium excretion

Answer

Correct answer : Inhibits osteoclast function

Denosumab is a RANKL inhibitor thereby inhibiting osteoclast function and survival and hence improving bone thickness.

Question 4

A 42 year old male presents with tiredness and general aches and pains. He has a past history of bipolar disorder for which he takes lithium and aripiprazole. He is also a type 2 diabetic for which he takes metformin. His investigations reveal the following:

		Normal Ranges
Calcium	2.86 mmol/l	(2.2 - 2.6)
Phosphate	0.78 mmol/l	(0.8 - 1.4)
PTH	11.2 pmol/l	(3 - 5.5)

Which of the following is the likely diagnosis?

- **A)** Drug induced hyperparathyroidism
- **B)** Familial hypocalciuric hypercalcaemia
- **C)** Pseudohypoparathyroidism
- **D)** Secondary hyperparathyroidism
- **E)** Tertiary hyperparathyroidism

Answer

Correct answer : Drug induced hyperparathyroidism

Lithium is a recognised cause of hyperparathyroidism although the mechanism is ill understood. Stopping therapy, if possible, may result in a resolution of the hyperparathyroidism although the condition may persist and may require surgery. If it is not possible to stop treatment, the hyperparathyroidism, often due to an adenoma, can be treated surgically and medication continued.

Question 5

A 56 year old female is referred as she has been concerned about osteoporosis. She went through the menopause uneventfully at the age of 50 and has no particular problems of note. She has a strong family history of osteoporosis. A DEXA scan that she had obtained privately reveals a T score of -2.3 at the hip and -2.0 at the lumbar spine. Her investigations reveal:

		Normal Ranges
Calcium	2.36 mmol/l	(2.2 - 2.6)
Alkaline Phosphatase	88 iu/l	(50 - 110)
PTH	8.6 pmol/l	(3 - 5.5)
Vitamin D	12.7 nmol/l	(>20)

Which of the following would be the most appropriate treatment for this patient?

- **A)** Calcium and vitamin D supplements
- **B)** Continuous combined HRT
- **C)** Raloxifene
- **D)** Teriparatide
- **E)** Weekly alendronate

Answer

Correct answer : Calcium and vitamin D supplements

This patient has secondary hyperparathyroidism and vitamin D deficiency and has osteopenia as evidenced by the DEXA T score greater than 2.5. In this scenario, the most appropriate initial treatment would be vitamin D replacement/Calcium treatment which would be expected to improve bone mineral density in the context of hypovitaminosis D. This can be reviewed with serial scanning.

CKS guidance

Question 6

A 45 year old woman is referred by her GP for investigation of her hypercalcaemia. He noted the following investigations:

		Normal Ranges
U+Es	Normal	
Calcium	2.8 mmol/l	(2.2 - 2.6)
Phosphate	1.0 mmol/l	(0.8 - 1.4)

The patient originally attended the GP with vague aches and pains which have been present for two months or so and she also admits to feeling rather depressed. She is only taking fluoxetine 20 mg daily at present. There is nil of note on examination. Further investigations reveal:

		Normal Ranges
PTH	4.4 pmol/l	(3 - 5)
Vitamin D	55 nmol/l	(>50)
Urine calcium	7 mmol/d	(0 - 7.5)

Which of the following is the likely diagnosis?

- **A)** Drug-induced
- **B)** Familial hypocalciuric hypercalcaemia
- **C)** Milk-Alkali syndrome
- **D)** Primary hyperparathyroidism
- **E)** Tertiary hyperparathyroidism

Answer

Correct answer : Primary hyperparathyroidism

This patient has mild hypercalcaemia, an inappropriately normal PTH concentration and has a normal/highish urine calcium excretion. The latter would argue against a diagnosis of FHH where urine calcium excretion is low (less than 5 mmol/d) and so the likely diagnosis is primary hyperparathyroidism.

Question 7

A 55 year old female presents with a one week history of sickness, lethargy and fatigue. She has a two year history of metastatic breast carcinoma. On examination, she appears dehydrated and unwell.
Her investigations reveal:

		Normal Ranges
Sodium	148 mmol/l	(134-144)
Potassium	4.8 mmol/l	(3.5-5)
Urea	12.8 mmol/l	(3-8)
Creatinine	180 micromol/l	(50-100)
Calcium	3.8 mmol/l	(2.2 - 2.6)

Which of the following is the most appropriate initial treatment for this patient?

- **A)** IV Calcitonin
- **B)** IV Dextrose
- **C)** IV Normal saline
- **D)** IV Pamidronate
- **E)** IV Prednisolone

Answer

Correct answer : IV Normal saline

This patient has marked hypercalcaemia as reflected by the calcium above 3 mmol/l. The most appropriate initial management of this patient with dehydration and hypercalcaemia which is likely to be malignancy related is IV rehydration with normal saline. One would not contemplate IV bisphosphonate until rehydration is completed as this would compound the nephrotoxicity.

Question 8

A 45 year old female is receiving 10 mg of prednisolone daily as a treatment of ophthalmic Graves' disease with the intention of her remaining on this dose for the next six months. Which is the most appropriate approach regarding potential osteo protection for this patient?

- **A)** Assess FRAX score
- **B)** Commence calcium and vitamin D supplements
- **C)** Commence weekly alendronate
- **D)** DEXA scan
- **E)** No treatment/further investigation required

Answer

Correct answer : Assess FRAX score

In a patient less than 50 years of age, any therapeutic intervention for osteo protection in association with steroid therapy should be guided initially by a FRAX score initially (1). The risk of 6 months of treatment on bone health of a 10mg dose would be considered to be low according to NICE guidance but studies do suggest that with doses above 5mg daily that BMD may decline. Therfore, based on the FRAX score DEXA may be required to monitor BMD during treatment but there is no need to rush in with osteoprotective therapies.

1. Practical guide to monitoring corticosteroid therapy

Question 9

A 17-year-old caucasian female is seen due to various aches and pains. She takes no medication other than the combined oral contraceptive. She has been generally well but has had general muscle aches for a couple of years. There is nothing to note on physical examination and she has normal height and normal secondary sexual characteristics. Her results reveal:

		Normal Ranges
Full blood count	Normal	
U+Es	Normal	
Calcium	1.96 mmol/l	2.2-2.6
Phosphate	1.68 mmol/l	0.7-1.2
PTH	68 nmol/l	3-5.5
Free T4	9.8 pmol/l	9-23
TSH	2.2 mu/l	0.5-5

Which of the following is the likely diagnosis?

- **A)** Factitious results
- **B)** Primary hypoparathyroidism
- **C)** Pseudohypoparathyroidism
- **D)** Pseudo-pseudohypoparathyroidism
- **E)** Secondary hyperparathyroidism

Answer

Correct answer : Pseudohypoparathyroidism

This young girl has a long history of muscle aches and pains and has a low calcium concentration but elevated phosphate. The latter is suggestive of a hypoparathyroidism rather than vitamin D deficiency (where a phosphate would be expected to be low). However, the patient has an elevated PTH concentration and so this would suggest an unresponsiveness to PTH and hence a diagnosis of pseudohypoparathyroidism. The fact that she has no skeletal abnormalities (short 4th Metacarpal for instance) would suggest a type 1b or type 2 pseudohypoparathyroidism.

Question 10

The following results were obtained on a DEXA scan of the hip of a 55 year old female who was concerned regarding her risk of osteoporosis since there was a strong family history of fragility fractures.

	BMD	T score	Z score
Neck	0.74	-1.5	-0.29
Trochanteric	0.73	+0.38	+1.1
Intertrochanteric	0.91	-1.29	-0.68
Total	0.83	-0.95	-0.11
Ward's triangle	0.50	-2.0	-0.21

Which of the following is the correct interpretation of this DEXA scan?

- **A)** Normal bone mineral density
- **B)** Osteomalacia
- **C)** Osteopenia
- **D)** Osteopetrosis
- **E)** Osteoporosis

Answer

Correct answer : Osteopenia

A DEXA scan measures bone mineral density (BMD) at various sites, typically the lumbar spine and hip are reported. The T score is the number of standard deviations of the patient's BMD and that of a 'young' control. The Z score is the number of standard deviations between the BMD of the subject and that expected for an aged and sex matched control.
T scores greater than -1 are normal. T scores between -1 to -2.5 reflect osteopenia and T scores less than -2.5 reflect osteoporosis. This DEXA report of the hip reveals T scores between +0.38 and -2.0 which indicate osteopenia at Ward's triangle and the intertrochanteric region.

Question 11

A 67 year old lady with newly diagnosed osteoporosis re-presents to clinic with intolerance to alendronate 70 mg weekly after 4 weeks of persistence. There is history of previous fracture at the left wrist when she fell off the fourth step of a ladder 4 years ago. She is also taking calcium and vitamin D supplementation. She underwent menopause at age 40 and did not take hormone replacement therapy. There is a family history of osteoporosis and hip fracture in her late mother. Other secondary causes of osteoporosis have been excluded.
Her DEXA scan T scores are:

AP Spine	-3.9
Total Hip	-3.3

Which treatment is appropriate as per NICE guidelines?

- **A)** Intravenous zoledronic acid
- **B)** Continue calcium and vitamin D supplementation alone
- **C)** Denosumab
- **D)** Ibandronate
- **E)** Teriparatide

Answer

Correct answer : Ibandronate

This question refers to the NICE guidelines for the secondary prevention of osteoporotic fractures which relates only to treatments for the secondary prevention of fragility fractures in postmenopausal women who have osteoporosis and have sustained a clinically apparent osteoporotic fragility fracture. Osteoporosis is defined by a T-score of -2.5 standard deviations (SD) or below on dual-energy X-ray absorptiometry (DXA) scanning.

Alendronate is recommended as a first line treatment option for the secondary prevention of osteoporotic fragility fractures in postmenopausal women who are confirmed to have osteoporosis. In this case the patient has severe osteoporosis, a previous fracture and is intolerant of alendronate. Therefore according to the guidance the patient should initially try an alternative bisphosphonate initially. Then, if intolerant an alternative should be considered, such as teriparatide, denosumab or IV bisphosphonates.

Question 12

According to the NIH consensus criteria, which of the following is an indication to operate in patients with primary hyperparathyroidism?

- **A)** Age > 50 years
- **B)** Corrected Calcium >2.75 mmol/L
- **C)** Osteopenia on BMD
- **D)** Worsening liver function
- **E)** Decrease in creatinine clearance by >30%

Answer

Correct answer : Decrease in creatinine clearance by >30%

According to the NIH consensus statement, the following parameters can be used as indications for parathyroidectomy in asymptomatic patients with primary hyperthyroidism:

- Age < 50 years
- T score of < -2.5 on bone mineral densitometry (BMD)
- Plasma calcium > 2.85 mmol/L
- Urinary calcium excretion of 10 mmol/d (or > 400 mg/day)
- Decrease in creatinine clearance by >30% as compared to age matched normal subjects

Other indications for parathyroidectomy in primary hyperparathyroidism include

- Symptomatic patient (definitive signs and symptoms of hypercalcaemia- such as proximal weakness, gait disturbance, hyper-reflexia)
- Evidence of end organ damage (renal failure, renal stones, osteitis fibrosa cystica and pancreatitis)

Question 13

A GP has referred a 42 year old gentleman with hypercalcaemia to the endocrine clinic with a probable diagnosis of primary hyperparathyroidism based on the following blood results:

		Normal Ranges
Corrected Calcium	2.75 mmol/L	(2.2-2.6)
Phosphate	0.7 mmol/L	(1-1.4)
25-OH Vitamin D	32 nmol/L	(desirable above 50)
PTH	7.2 pmol/L	(1.0-6.0)

Which of the following results/ observations will go against the suggested diagnosis?

- **A)** A family history of hypercalcaemia
- **B)** Calcium excretion of > 50 mg/ day
- **C)** History of renal stones
- **D)** Normal renal function
- **E)** Patient on thiazide diuretics

Answer

Correct answer : A family history of hypercalcaemia

This is a common scenario of where the GP refers a patient with suspected hyperparathyroidism but it may be Familial Hypocalciuric Hypocalcaemia. Primary HPTH would be suggested by a calcium excretion above 50 mmg/day but the family history would be more in keeping with FHH. Familial hypocalciuric hypercalcaemia (FHH) is an autosomal dominant condition secondary to a mutation of the calcium-sensing receptor leading to a decreased excretion of calcium from the body, with an end result of mild hypercalcaemia. It is a benign disorder and an important differential diagnosis for primary hyperparathyroidism (PHT). The key distinguishing features include:

- A family history of mild hypercalcaemia
- No evidence of end organ damage (normal renal function, absence of nephrolithiasis, no evidence of bone disease)
- Decreased 24 hour urinary calcium excretion (<50 mg/day or < 2.5 mmol/day) or fasting calcium/creatinine excretion ratio of < 0.01

Question 14

A 67 year old woman comes to see you in osteoporosis clinic. She has had 2 vertebral fractures in the past. Her GP has given her alendronate and risedronate but she developed oesophagitis with both. She was taking strontium ranelate which was withdrawn and now continues on raloxifene together with calcium and vitamin D. Her DEXA scan was repeated and shows that her T-score at the lumbar spine has fallen from -2.8 to -3.5 and at the neck of the femur it is stable at -3.6.

Which of the following management options would you select for the management of this patient?

- **A)** Continue current treatment unchanged
- **B)** Start IV zolendronate
- **C)** Start denosumab
- **D)** Start ibandronate
- **E)** Start teriparatide

Answer

Correct answer : Start teriparatide

NICE guidelines recommend the use of teriparatide for secondary osteoporosis in women who are unable to take bisphosphonates or have a contraindication to, or are intolerant of, alendronate and either risedronate or etidronate; or who have had an unsatisfactory response to treatment with bisphosphonates and who are 65 years or older and have a T-score of - 4.0 SD or below, or a T-score of - 3 SD or below plus more than two fractures, or who are aged 55-64 years and have a T-score of -4 SD or below plus more than two fractures.

Reference:

- https://www.nice.org.uk/guidance/ta161

Question 15

A 65 year old gentleman presents with deformity and some discomfort in his tibia. His bloods show raised alkaline phosphatase with normal calcium and phosphate levels. His skull and spinal X rays confirm the diagnosis of Paget's disease. Which one of the following is the most appropriate treatment for his underlying condition?

- **A)** IV pamidronate
- **B)** IV zoledronate
- **C)** Oral calcium carbonate and vitamin D
- **D)** Oral risedronate
- **E)** Oral cinacalcet

Answer

Correct answer : IV zoledronate

The prevalence of Paget's disease is about 2% over the age of 55 years in the UK. Only 1 out of 10 patients are symptomatic. The indications for treating Paget's disease include presence the of symptoms (pain), deformity, complications (such as deafness, spinal cord compression) and hypercalcaemia. Bisphosphonates form the mainstay for the treatment. The bisphosphonates licensed for treatment in Paget's disease include pamidronate, risedronate, etidronate, tiludronic acid and zolendronate. Out of these zolendronate has the longest duration of action, often only a single dose is required for treatment purposes and has greater efficacy in reducing alkaline phosphatase vs oral risedronate.

Question 16

A 72 year old gentleman presents with a painful lower leg. Examination of the left leg reveals thickening and bowing of the tibia which is slightly warmer to touch over this than the right. His investigations reveal an alkaline phosphatase of 450 iu/l (50-110), ALT of 22 iu/l (10-50) and a calcium of 2.3 mmol/l (2.2-2.6).

Which of the following is the most appropriate next investigation to establish the suspected diagnosis?

- **A)** Bone biopsy
- **B)** Bone densitometry
- **C)** Bone scan
- **D)** MRI tibia
- **E)** X-ray of tibia

Answer

Correct answer : X-ray of tibia

As about 90% of patients with Paget's disease are usually asymptomatic, the diagnosis is often incidental based on radiological findings. In the early stages, the lesions seen are mostly osteolytic, and in tubular long bones begin in the metaphysic and migrate down the shaft in a V shaped 'cutting cone'. As the disease progresses, mixed lytic and sclerotic lesions are seen including trabecular thickening and increased density. In later stages, most of the lesions are sclerotic. Although isotope bone scanning is a useful investigation to assess the extent of disease and bone biopsy it is used only occasionally to confirm the diagnosis, with X-ray of afflicted bone often the most useful initial diagnostic test.

Question 17

A 62 year old lady with a previous history of fracture of the forearm and spine presents with a mechanical fall leading to a fracture of the ulnar bone. She is already on alendronate 70 mg weekly. Her bone mass density (BMD) profile shows severe osteoporosis (Z value < -3.5- -4.5). What is the next best therapeutic option for her treatment?

- **A)** Ibandronate IV
- **B)** Raloxifene
- **C)** Strontium
- **D)** Teriparatide
- **E)** Zoledronate IV

Answer

Correct answer : Teriparatide

Teriparatide is recommended for treatment of severe osteoporosis (osteoporosis in the presence of 1 or more fragility fractures) in patients in whom treatment with bisphosphonates has been unsatisfactory. The high cost associated with this agent restricts their use to only a selective group of patients. Teriparatide is contraindicated in the presence of renal impairment (eGFR < 30 mL/minute/ 1.73 m^2), severe hepatic impairment, hypercalcaemia, metabolic bone disease (Paget's disease, primary hyperparathyroidism) and an unexplained rise in alkaline phosphatase levels.

Reference:

- Guideline for the diagnosis and management of osteoporosis in postmenopausal women and men from the age of 50 years in the UK, Produced by JA Kanis, J Compston, A Cooper, C Cooper, R Francis, D Marsh, EV McCloskey, D Reid, P Selby and M Wilkins, on behalf of the National Osteoporosis Guideline Group (NOGG).

Question 18

A new experimental drug is being introduced for the treatment of osteoporosis. It has been shown to act by inhibiting production of RANKL factor. Which of the following cells is responsible for the production of RANKL?

- **A)** Lining cells
- **B)** Marrow cells
- **C)** Osteoblasts
- **D)** Osteoclasts
- **E)** Osteocytes

Answer

Correct answer : Osteoblasts

The communication between osteoblasts and osteoclasts seems to occur as a result of locally produced signals which include osteoclast differentiation factor called RANK ligand (RANKL) and osteoprotegerin (OPG). RANKL is a protein derived from osteoblasts, which binds to the RANK receptor and activates NF-kB on the surface of osteoclast precursors leading to increased osteoclast production.

OPG in contrast binds to RANKL and inhibits its interaction with the RANK receptor. Therefore inhibition of RANKL factor leads to down regulation of osteoclast production. The monoclonal antibody, Denosumab is a RANKL inhibitor and thereby inhibits osteoclast recuitment, action and proliferation

Denosumab

Question 19

A 70 year old man with rheumatoid arthritis is on a long term steroid therapy (prednisolone-7.5 mg per day). At what range of T scores on bone mineral densitometry (BMD) will you consider starting him on bisphosphonates?

- **A)** Start bisphosphonate irrespective of T score
- **B)** T score < -1
- **C)** T score < -1.5
- **D)** T score < -2
- **E)** T score< -2.5

Answer

Correct answer : Start bisphosphonate irrespective of T score

This gentleman has two clinical risk factors (CRFs) for development of osteoporosis- rheumatoid arthritis and usage of steroids. Both of these are moderate risk factors for the development of osteoporosis in contrast with smoking and alcohol intake which are considered weak CRFs. A parental history of hip fracture and previous fragility are generally classified as strong risk factors for osteoporosis development. SIGN and NICE Guidelines suggest that with this long term dose at 7.5 mg/d, the patient should be commenced on a bisphosphonate. This is with a dose of 7.5mg/d or above for 3 months or more.

Question 20

A 71-year-old man is admitted with cramps and twitching which have deteriorated over the last 2 weeks. He denies any change in bowel habit, and has a past history of type 2 diabetes and hypertension. He was taking metformin and recently started sitagliptin. He also takes bendrofluazide, ramipril and omeprazole for GORD.

On examination, trousseau's sign was positive, his pulse was 88bpm and blood pressure 128/88 mmHg.

His investigations revealed:

Sodium	142 mmol/l	(134-144)
Potassium	3.5 mmol/l	(3.5-5.5)
Urea	5.5 mmol/l	(3-8)
Creatinine	80 micromol/l	(50-100)
Calcium	1.80 mmol/l	(2.2-2.6)
Phosphate	0.8 mmol/l	(0.7-1.5)
PTH	5 pmol/l	(3.5-5.5)
HbA1c	55 mmol/mol	(<48)

Which of the following is most likely responsible for this patient's presentation?

- **A)** Bendrofluazide
- **B)** Gitelman's syndrome
- **C)** Omeprazole
- **D)** Sitagliptin
- **E)** Ramipril

Answer

Correct answer : Omeprazole

Explanation

The patient has severe hypocalcaemia, a lowish phosphate, and a slightly raised PTH which is inappropriate for this level of hypocalcaemia. This suggests a PPI induced hypomagnesaemia associated with hypoparathyroidism and hypocalcemia. Bendrofluazide is likely to cause hypercalcaemia, but may well exacerbate the hypomagnesemia associated with the PPI. It's important in this scenario to measure the magnesium which will be low.

References:

- Sivakumar, J. (2016) 'Proton pump inhibitor-induced hypomagnesaemia and hypocalcaemia: case review', International journal of physiology, pathophysiology, 8(4), pp. 169–174.

Question 21

A 62-year-old woman is admitted to MAU through her GP as she has become increasingly unwell over the last few days. She is lethargic, has had occasional episodes of abdominal pain, and is clinically dehydrated. She has a recent history of metastatic breast cancer with bony involvement, for which she is receiving palliative treatment. Her results reveal:

		Normal Ranges
Sodium	144 mmol/l	(134-144)
Potassium	3.1 mmol/l	(3.5-5.5)
Calcium	4.1 mmol/l	(2.2-2.6)

Which of the following would you expect to find on the ECG?

- **A)** Prolonged PR Interval
- **B)** QT shortening
- **C)** ST elevation
- **D)** Tall tented T waves
- **E)** Widened QRS complexes

Answer

Correct answer : QT shortening

The abnormality here will relate to the markedly elevated calcium. The QT interval is typically shortened in hypercalcaemia. Other features in severe hypercalcaemia include J waves and bizarre QRS appearance.

- Some examples of ECG abnormalities in hypercalcaemia

Question 22

A 68 year old caucasian woman attends clinic with a fractured humerus following an innocuous fall. She has no other risk factors. Her total hip T-score is -3.4 and spine T-score is -3.1. Her FRAX score for hip fracture is 12% and for a major fracture is 30%. Which of the following would be the most appropriate approach to the management of this patient?

- **A)** Alendronate
- **B)** Calcitriol
- **C)** Calcium and vitamin D supplement
- **D)** Denosumab
- **E)** No treatment required

Answer

Correct answer : Alendronate

No treatment is an inadvisable option because plentiful data show that patients with osteoporosis and a previous fragility fracture will have a reduced risk of a new fracture if treated with pharmacological therapy (National Osteoporosis Foundation. Clinician's guide to prevention and treatment of osteoporosis. Washington, DC: NOF; 2014)

Calcitriol is incorrect. It has been approved by the FDA for use in renal dialysis patients and hypoparathyroidism but there are no reliable data to demonstrate its use in reduction of osteoporotic fractures. Alendronate is the correct answer. This agent is approved for prevention and treatment of postmenopausal osteoporosis; and to increase bone mass in men with osteoporosis; and for treatment of osteoporosis in men and women taking glucocorticoids.

Question 23

A 70 year old woman is being followed up in clinic She initially presented with a fractured humerus. Her total hip T-score was -3.4 and spine T-score -3.1 at presentation. Her FRAX score for hip fracture was 12% and for major fracture was 30%. After two years of treatment with Alendronate, calcium and vitamin D, her total hip T-score improved to -3.2. What is the probability of her reaching a T-score >-2.5 in the next three years.

- **A)** <5%
- **B)** 7.5%
- **C)** 10%
- **D)** 15%
- **E)** 20%

Answer

Correct answer : <5%

The correct answer is a, <5%. Treatment should offer a 50% or greater chance of achieving the treatment goal within 3-5 years. If not, then a more potent treatment should be considered. If the goal is low fracture risk then the patient’s initial assessment should include a risk assessment by a validated method such as FRAX. The goal should be substantially better than the treatment threshold.

Question 24

A 70 year old woman with osteoporosis is being treated with alendronate, plus calcium and vitamin D supplementation. After two years of treatment, she falls out of bed and is found to have fractured both her distal radius and her proximal humerus. Bone resorption as measured by CTX was not elevated at baseline. Her BMD and her CTX are essentially unchanged since she started treatment. This may be defined as treatment failure, according to the International Osteoporosis (IOF) working group, but which component of her clinical picture defines it as a treatment failure?

- **A)** One incident fragility fracture
- **B)** Two or more incident fragility fractures
- **C)** Either a significant reduction in beta CTX or a significant decrease in BMD
- **D)** Elevated beta CTX at baseline and no significant reduction in BMD during treatment
- **E)** Elevated beta CTX at baseline and a significant decrease in BMD during treatment

Answer

Correct answer : Two or more incident fragility fractures

The correct answer is b, two or more incident fractures. For further discussion, see A Diez-Perez et al. Osteoporosis International 2012; 23: 2769-74.

A fragility fracture occurs after less trauma than might be expected to fracture a normal bone. Fracturing upon falling out of bed is a typical example of a fragility fracture. As regards option a, one incident fragility fracture alone, without changes in biomarkers of BMD, is not viewed as treatment failure. As regards options d and e, changes in biomarkers or BMD alone are not viewed as treatment failure unless the patient also has an incident fracture. As regards option c, both criteria are needed for the response to be classified as a treatment failure.

The IOF states that treatment has failed if any of these occurs:

- Two or more incident fragility fractures
- One incident fracture and elevated serum CTX or P1NP at baseline and either no significant reduction in resorption biomarkers at baseline or a significant decrease in BMD
- Both no significant decrease in CTX or P1NP and a significant decrease in BMD

Elderly patients are at risk of falls due to factors such as poor coordination, poor vision, muscle weakness and confusion. Educating patients about the risk of falls and fractures and modifying the home environment for safety are important. For further discussion, see http://www.iofbonehealth.org/what-sarcopenia

Question 25

A 72 year old female patient attends to discuss her Osteoporosis (T score of -3.0) which was diagnosed 16 months previously following a wrist fracture. At that time she was commenced on once weekly Alendronate plus calcium and Vitamin D supplements.

She has not had other fractures, is not on oral steroid medication and does not suffer with any other relevant medical condition. She enquires as to whether she can have another DXA scan to see if the treatment is working?

What is the advice for repeating a DXA scan?

- **A)** DXA is repeated 6 M after initiation of treatment
- **B)** DXA scan is repeated every year
- **C)** Review DXA every 5 years
- **D)** Review DXA 2-5 years from previous scan if it is likely to influence management
- **E)** Review DXA 5-7 years from previous scan

Answer

Correct answer : Review DXA 2-5 years from previous scan if it is likely to influence management

Review the DXA scan 2-5 years after previous scan if it is likely to influence management. DXA scans are of limited value in assessing response to treatment. This is because the changes in BMD in response to treatment are small and slow and similar in magnitude to the error of the DXA measurement. The decision as to whether and when to repeat a DXA scan will depend on the initial results and the individual patient's circumstances.

Question 26

A 69 year old woman is diagnosed with two vertebral fractures, without a history of injury. Past history is of a fragility fracture to the forearm and Osteoporosis (T score of -3.8 at hip) which were diagnosed four years previously. She has been on a Bisphosphonate medication for 4 years. She is adherent and complying with the instructions for administration of the bisphosphonate. She suffers with Asthma and type 2 Diabetes, is not prescribed any other relevant medications and is active with a normal gait.
Which first line intervention would you advise?

- **A)** Anti-tissue transglutaminase (tTG) antibodies
- **B)** Blood glucose
- **C)** FRAX score
- **D)** Repeat DXA scan
- **E)** U+Es

Answer

Correct answer : Repeat DXA scan

DXA scan and arrange a range of investigations. Obtaining a current BMD on DXA could influence management. Further blood investigations should be considered to ensure that other diseases that mimic or cause Osteoporosis, bone fragility and fracture have not been missed. All else being well, deterioration of T score on DXA, plus refracture may signify an unsatisfactory response to treatment and would warrant consideration for change in bone medication. As the patient has had a number of fractures (including vertebral) and a poor T score for her age, she may meet the NICE guidelines for Teriparatide, an anabolic bone medication (NICE Secondary Prevention of Fractures:TA 161 (2008))

NICE defines an unsatisfactory response to treatment as occurring when a patient has another fragility fracture despite adhering fully to treatment for longer than 1 year and there is evidence of a decline in BMD. Teriparatide is recommended for patients of 65 years and over who have a T score of -4.0 SD or worse, or a T score of -3.5 SD or worse plus more than two fractures, or who are aged 55 to 64 years and have a T score of -4SD or below plus more than two fractures. This patient would be considered for referral to a consultant bone specialist.

Question 27

A 77-year-old man is referred by the GP with polyuria and fatigue. His calcium has been noted to be 3.1 mmol/l (2.2-2.6) with a PTH of 13.5 pmol/l (3.5-6). He has a past history of ischaemic heart disease, having had previous stenting and associated NYHA stage 3 heart failure. Repeat investigations confirm the GP's results. He has a urea of 13.8 mmol/l (3-8), with a creatinine of 168 micromol/l (50-100).

He is adamantly opposed to surgical intervention and at the MDT, the surgeons feel that surgical risk is rather high. Which of the following would be the most appropriate approach to the management of this patient?

- **A)** Intra-tumoural alcohol injection
- **B)** IV zoledronate
- **C)** Oral cinacalcet
- **D)** Subcutaneous calcitonin
- **E)** Weekly subcutaneous denosumab

Answer

Correct answer : Oral cinacalcet

This patient is not considered suitable for surgical intervention due to CV risk, and with the patient being opposed to surgery, the most appropriate approach to long term management would be the calcimimetic, cinacalcet. It acts like calcium on the calcium sensing receptor, thereby reducing PTH levels.

Cinacalcet

Question 28

A 40-year-old woman is referred to clinic by her GP as she has been complaining of fatigue. He checked some of her test results, which revealed the following:

		Normal Ranges
Calcium	2.78 mmol/l	(2.2-2.6)

On questioning she has been feeling general fatigue and feels a little down. There is no particular family history of note. There is nothing of note on examination.
Further investigations reveal the following:

		Normal Ranges
Calcium	2.81 mmol/l	
Phosphate	1.1 mmol/l	(0.8-1.4)
PTH	5 pmol/l	(3-5.5)
24hr urine calcium	88 mg/d	(50-300)
Calcium creatinine clearance ratio	0.018	(>0.02)
DEXA T-scores	-1 to -1.8	

Which of the following would be the most appropriate approach to the management of this patient?

- **A)** Arrange Sestamibi scan
- **B)** MRI neck and chest
- **C)** Request calcium sensing receptor mutational analysis
- **D)** Surgical neck exploration
- **E)** Therapeutic trial cinacalcet

Answer

Correct answer : Request calcium sensing receptor mutational analysis

In this patient, she has symptoms and an elevated calcium with normal PTH. This would indeed suggest primary hyperparathyroidism BUT: this patient has a lowish 24hr calcium excretion of 88 mg/d (<100) and appropriately has had a calcium creatinine clearance ratio measured which is below 0.02 suggesting that the diagnosis is familial hypocalciuric hypocalcaemia rather than primary hyperparathyroidism. The next step would be analysis for mutations of the calcium sensing receptor known to cause FHH. This 2 step process has a diagnostic sensitivity for FHH of 98%.

Familial hypocalciuric hypercalcaemia: a review. Christensen SE1, Nissen PH, Vestergaard P, Mosekilde L.

Question 29

A 49-year-old woman is referred by the GP with a high calcium of 2.7, which is picked up on routine bloods as part of an insurance medical.
She is otherwise asymptomatic. Investigations reveal:

		Normal Ranges
Calcium	2.69 mmol/l	(2.2-2.6)
PTH	10.2 pmol/l	(3 – 5.5)
Vitamin D	70 nmol/l	(>50)
24hr urine calcium	350 mg/d	(50-300)
DEXA T scores	- 0.5 to -1.8	

Which of the following would be the most appropriate approach to the management of this patient?

- **A)** Monitor
- **B)** Reassure and discharge
- **C)** Recommend parathyroid surgery
- **D)** Treat with alendronate
- **E)** Treat with cinacalcet

Answer

Correct answer : Recommend parathyroid surgery

This woman has asymptomatic primary hyperparathyroidism with elevated calcium and PTH and elevated urine calcium concentrations. As she is under 50, NIH guidelines recommend surgery. Other reasons for surgery in asymptomatic primary hyperparathyroidism include Ca >2.85 mmol/l, a T score at any site <-2.5 and eGFR <60 ml/min.

Guidelines for the Management of Asymptomatic Primary Hyperparathyroidism: Summary Statement from the Third International Workshop John P. Bilezikian, Aliya A. Khan, John T. Potts, Jr, and on behalf of the Third International Workshop on the Management of Asymptomatic Primary Hyperthyroidism

Question 30

A 68 year old caucasian woman attends clinic with a fractured humerus following an innocuous fall. She has no other risk factors. Her total hip T-score is -3.4 and spine T-score is -3.1. Her FRAX score for hip fracture is 12% and for a major fracture is 30%. Which of the following would be the most appropriate approach to the management of this patient?

- **A)** Alendronate (oral bisphosphonate)
- **B)** Calcitriol
- **C)** Calcium and vitamin D supplement
- **D)** Genistein
- **E)** No treatment required

Answer

Correct answer : Alendronate (oral bisphosphonate)

No treatment is an inadvisable option because plentiful data show that patients with osteoporosis and a previous fragility fracture will have a reduced risk of a new fracture if treated with pharmacological therapy (National Osteoporosis Foundation. Clinician's guide to prevention and treatment of osteoporosis. Washington, DC: NOF; 2014)

Calcitriol is incorrect. It has been approved by the FDA for use in renal dialysis patients and hypoparathyroidism but there are no reliable data to demonstrate its use in reduction of osteoporotic fractures. Genistein is incorrect. More data are needed to understand the effects of this isoflavone phytoestrogen on fracture risk and bone health. Alendronate is the correct answer. This agent is approved for prevention and treatment of postmenopausal osteoporosis; and to increase bone mass in men with osteoporosis; and for treatment of osteoporosis in men and women taking glucocorticoids.

Question 31

A 70 year old woman is being followed up in clinic She initially presented with a fractured humerus. Her total hip T-score was -3.4 and spine T-score -3.1 at presentation. Her FRAX score for hip fracture was 12% and for major fracture was 30%. After two years of treatment with Alendronate, calcium and vitamin D, her total hip T-score improved to -3.2. What is the probability of her reaching a T-score >-2.5 in the next three years.

- **A)** <5%
- **B)** 7.5%
- **C)** 10%
- **D)** 15%
- **E)** 20%

Answer

Correct answer : <5%

The correct answer is a, <5%. Treatment should offer a 50% or greater chance of achieving the treatment goal within 3-5 years. If not, then a more potent treatment should be considered. If the goal is low fracture risk then the patient’s initial assessment should include a risk assessment by a validated method such as FRAX. The goal should be substantially better than the treatment threshold.

Question 32

A 56 year old caucasian female returns to clinic. She had presented with various aches and pains. She was obese and was known to have osteoarthritis of the hips. The following investigations return and you discuss them with the patient:

U+Es	Normal	
ESR	15 mm/hr	(0-10)
Fasting glucose	6.2 mmol/l	(3.5-5.6)
Calcium	2.3 mmol/l	(2.2 – 2.6)
Phosphate	1.2 mmol/l	(0.8 – 1.5)
Alkaline phosphatase	125 IU /l	(50-110)
AST	38 IU /l	(0-50)
ALT	35 IU /l	(0-50)
PTH	9.8 pmol/l	(3.5-6)

What is the likely explanation for her presentation and these results?

- **A)** Drug-induced
- **B)** Polymyalgia rheumatica
- **C)** Primary hyperparathyroidism
- **D)** Tertiary hyperparathyroidism
- **E)** Vitamin D deficiency

Answer

Correct answer : Vitamin D deficiency

This middle-aged and obese female has an elevated PTH concentration, slightly raised alkaline phosphatase with normal calcium and phosphate. These results, together with the history of aches and pains would suggest a diagnosis of vitamin D deficiency. Both PTH and vitamin D work together to maintain calcium concentrations. With a vitamin D deficiency, a **secondary hyperparathyroidism** (Journal of Royal Society of Medicine (2004) 97(7): 322–325 Routine biochemistry in suspected vitamin D deficiency) occurs to continue to maintain the normal calcium. The vitamin D concentration could be assessed if it is felt to be required but there is a rationale for treatment alone as this patient is symptomatic.

The NOS Guidelines state that where rapid correction of vitamin D deficiency is required, such as in patients with symptomatic disease or about to start treatment with a potent antiresorptive agent (zoledronate or denosumab), the recommended treatment regimen is based on fixed loading doses followed by regular maintenance therapy. A loading regimen to provide a total of approximately 300,000 IU vitamin D, given either as separate weekly or daily doses over 6 to 10 weeks, and maintenance therapy comprising vitamin D in doses equivalent to 800–2000 IU daily (occasionally up to 4,000 IU daily), given either daily or intermittently at higher doses. (Francis, Prof. R et al, (2013) Vitamin D and Bone Health: A Practical Clinical Guideline for Patient Management. The National Osteoporosis Society)

In this case she also has impaired fasting glucose and the recommendation (Patient.co.uk (2012) Glucose Toletrance Tests) would be to refer for an oral glucose tolerance test too.

Francis, Prof. R et al, (2013) Vitamin D and Bone Health: A Practical Clinical Guideline for Patient Management. The National Osteoporosis Society.

Question 33

An 80 year old male is reviewed after having been admitted to hospital with a fall. He has been getting rather weaker over the last few years and does find some difficulty rising from a chair. He lives alone since his wife died two years ago but has family support and carers twice daily. He is treated with amlodipine 5 mg daily, simvastatin 20 mg daily and aspirin 75 mg daily. His blood pressure is 138/70 mmHg without a postural fall. The only noticeable result amongst his investigations is the following:

25OH Vitamin D	8 nmol/l (<50)

Which of the following clinical features would you expect to find in association with this?

- **A)** Distal myopathy
- **B)** Neuropathy
- **C)** Pale conjunctivae
- **D)** Proximal myopathy
- **E)** Tetany on inflation of a blood pressure cuff

Answer

Correct answer : Proximal myopathy

This patient has severe vitamin D deficiency as indicated by the 25OHD vitamin D concentration less than 30 nmol/l. It has been demonstrated that below this level there is considerable impact on bone mineralisation, plus osteomalacia can occur. In conjunction with the effect on bone, vitamin D is associated with calcium influx into muscle, thus vitamin D deficiency is associated with a proximal myopathy. This may contribute to the difficulty rising from the chair that this patient experiences and also the issue of increasing falls.

Evidence suggests a reduction in **falls** following appropriate treatment.

BMJ 339:b3692 (2009) Fall prevention with supplemental and active forms of vitamin D: a meta-analysis of randomised controlled trials.

Although we are not told about his calcium level, one would assume from the results that these are normal. However, it would also be important to assess his calcium intake as the co-prescription of a calcium supplement may be required if his nutritional intake is less than 800mg daily.

Vitamin D deficiency is very common in the elderly with virtually every institutionalised elderly person being deficient. The reason for this is two-fold. Firstly, the elderly, particularly the institutionalised person is not exposed to sunlight to manufacture vitamin D and secondly the manufacture of vitamin D declines as we age. Current NOS guidelines recommend that all people over the age of 65 take a daily supplement containing 10mcg (400 IU) of vitamin D.

Francis, Prof. R et al, (2013) Vitamin D and Bone Health: A Practical Clinical Guideline for Patient Management. The National Osteoporosis Society.

Question 34

A 30 year old Asian male presents to clinic complaining of various muscle aches and pains. He is otherwise fit and well. He does not smoke and drinks about 10 units of alcohol weekly. He is employed as a junior doctor in the local hospital. Results reveal:

Calcium	2.35 mmol/l (2.2-2.6)
Phosphate	1.1 mmol/l (0.8-1.5)
PTH	9.8 pmol/l (3.5-6)
25OH Vitamin	10 nmol/l (>50)

Which of the following would be the most appropriate approach to the management of this patient?

- **A)** Advice plus combined calcium and vitamin D3
- **B)** Advice plus vitamin D3 800 IU/d
- **C)** Advice plus vitamin D3 1,000 - 2,000 IU/d
- **D)** Advice plus vitamin D3 300,000 IU given over 6-10 weeks
- **E)** Lifestyle advice only regarding nutritional intake and sun

Answer

Correct answer : Advice plus vitamin D3 300,000 IU given over 6-10 weeks

This patient has vitamin D deficiency as defined by a 25OH vitamin of less than 30 nmol/l (12 mcg/l). As he is symptomatic, the most appropriate approach is a treatment dose of vitamin D3 with a cumulative dose of 300,000 IU given as weekly split doses or daily split doses. Regimes include 50,000 IU given weekly over 6 weeks or 4,000 IU given daily over 10 weeks (Francis, Prof. R et al, (2013) Vitamin D and Bone Health: A Practical Clinical Guideline for Patient Management. The National Osteoporosis Society.) Smaller doses will not correct the deficiency appropriately as typically a dose of 1,000 IU of oral vitamin D daily will increase the 25OH vitamin D concentration by approximately 25 nmol/l (10 mcg/l). Higher doses may be required in certain groups such as the elderly or those taking liver inducing drugs eg anticonvulsants.

Advice alone is unlikely to raise 25OH vitamin D concentrations as generally there is not enough vitamin D in our food and also the sun in the UK at our latitude cannot generate enough vitamin D between Sept – May. In this Asian man who works in a hospital it is unlikely that he is exposed to sufficient sunlight. Vitamin D deficiency is well described in (Wiley online Library (2011) Summer and winter prevalence of vitamin D deficiency of young resident doctors in North India). This is likely to be true of a lot of healthcare workers and indeed any other group mostly working indoors.

If as is typically the case, the patient has an adequate vitamin D intake there is no point in using additional calcium supplementation. In fact with the dose of vitamin D being 400 IU and calcium of 500 - 600mg per tablet co-prescribing 5 or more of these tablets per day to replace vitamin D will result in excessive calcium intake.

Cardiff and Vale University Health Board (2013) Diagnosis and Management of Vitamin D Deficiency in children and adults, guidelines.

Question 35

A 45-year-old woman returned from a holiday to Tenerife. She had non-specific symptoms of being generally unwell and lethargy. She denied any history of weight loss or loss of appetite. She had no past medical history of note. She was not taking any medication. She smokes 30 cigarettes per day and she occasionally drinks alcohol. She did not have any significant family history. On examination, her general and systemic examination was unremarkable. FBC, U&E and LFTS were normal.

	Results	Normal Range
Serum corrected calcium	4.22 mmol/l	2.20 -2.60 mmol/l
Serum phosphate	1.2 mmol/l	0.8–1.4 mol/l
PTH	2.9 pmol/l	3.3- 8 pmol/l
25 (0H) Vitamin D levels	65 nmol/l	45–90 nmol/l

CT thorax, abdomen and pelvis were reported as normal.
Serum ACE levels were normal.
The acute hypercalcaemia was managed with fluids and bisphosphonates. What is the next step in investigating this patient?

- **A)** 1, 25-OH vitamin D levels
- **B)** Bone marrow biopsy
- **C)** FDG PET
- **D)** MRI abdomen
- **E)** Ultrasound parathyroid glands

Answer

Correct answer : 1, 25-OH vitamin D levels

Explanation:

This patient had very high serum corrected calcium with suppressed PTH levels. CT thorax, abdomen and pelvis reliably exclude malignancy in the majority of cases. The next step is to rule out granulomatous diseases such as sarcoidosis. Sarcoid granulomas can produce excessive level of active vitamin D. Therefore, 1,25(OH) vitamin levels should be obtained first before considering expensive/invasive investigations such as PET scan/bone marrow. Of note, serum ACE levels can be normal in up to 50 % of cases of sarcoidosis.

Reference:

- Conron, M., Young, C. and Beynon, H.L.C., 2000. Calcium metabolism in sarcoidosis and its clinical implications. Rheumatology, 39(7), pp.707-713

Question 36

A 39-year-old woman presented with symptoms of polyuria and polydipsia. She had non-specific symptoms of being generally unwell and lethargic. She denied history of weight loss or loss of appetite. She had no past medical history of note. She was not taking any medication. She smokes 30 cigarettes per day and she occasionally drinks alcohol. She did not have any significant family history. On examination, her general and systemic examination was unremarkable. FBC, U&E and LFTS were normal.

	Results	Normal Range
HbA1C	32 mmol/mol	<48 mmol/mol
Serum corrected calcium	3.92 mmol/l	2.20 -2.60 mmol/l
Serum phosphate	1.2 mmol/l	0.8–1.4 mmol/l
PTH	2.9 pmol/l	3.3- 8 pmol/l
25 (0H) Vitamin D levels	75 nmol/l	45–90 nmol/l
1, 25 - OH vitamin D levels	219.2 pmol/l	48-120 pmol/l
Serum ACE levels	Normal	

CT thorax, abdomen and pelvis were reported as normal.
Acute hypercalcaemia was managed with fluids and bisphosphonates.
What is the most likely underlying diagnosis?

- **A)** Ectopic PTH secretion
- **B)** Lymphoma
- **C)** Metastatic disease
- **D)** Primary hyperparathyroidism
- **E)** Sarcoidosis

Answer

Correct answer : Sarcoidosis

Explanation:

This patient had very high serum corrected calcium with suppressed PTH levels. In majority of the cases hypercalcaemia is due to either malignancy or primary hyperparathyroidism. CT thorax, abdomen and pelvis excluded malignancy. A very high level of active vitamin D levels in this patient is in keeping with sarcoidosis. Sarcoid granulomas can produce excessive levels of active vitamin D.

Reference:

- Conron, M., Young, C. and Beynon, H.L.C., 2000. Calcium metabolism in sarcoidosis and its clinical implications. Rheumatology, 39(7), pp.707-713

Question 37

A 61-year-old lady was referred to endocrine clinic with high calcium. She was completely asymptomatic. She had a past medical history of bipolar disorder and fragility fracture. She had been taking lithium for 17 years for bipolar disorder. Her mood has been stable on lithium. She is a smoker of 12 cigarettes per day. Her general and systemic examination was unremarkable.
Her blood tests are as follows:

		Normal Ranges
Calcium	2.89	2 - 2.6 mmol/L
Phosphate	0.97	0.8 - 1.5 mmol/L
PTH	14.9	1.6 - 7.2 mmol/L
Vitamin D	50	>69
Dexa scan	Osteoporosis of lumbar spine	

The most likely underlying diagnosis was lithium induced primary hyperparathyroidism. What is the next step in management?

- **A)** Admit and hydrate
- **B)** Cinacalcet
- **C)** Conservative management only
- **D)** Parathyroidectomy
- **E)** Stop Lithium

Answer

Correct answer : Parathyroidectomy

Explanation:

Lithium can cause hypercalcemia in about 10 to 20 percent of the cases and in the majority of the cases it is mild. This is likely due to increased secretion of PTH due to increase in the set point at which calcium suppresses PTH release. It also increases the serum magnesium and decreases urinary calcium and magnesium concentrations similar to FHH. The median duration of developing adenomas was 2 years. Hypercalcemia may resolve with in 1 to 4 weeks on stopping lithium. Normalisation of calcium depends on the duration. Calcium is unlikely to normalise in patients receiving lithium for more than 10 years. In this lady with primary hyperparathyroidism and end organ damage (osteoporosis), parathyroidectomy is advised. Her calcium is unlikely to normalise on stopping Lithium as she had been taking it for more than 10 years.

Question 38

A 70-year-old female is referred to emergency admissions by her GP. She had been feeling fatigued for 2 months or so and her GP had checked a few blood tests, all of which were normal. However, after another visit, he had checked her calcium and found this to be 2.75 mmol/l (2.2-2.6). He referred her in to acute medicine.

There was nothing else of note in her history other than tiredness and she had put on roughly 3 kg in weight over the last year. She took vitamin D supplements and sertraline 100 mg daily.

There was nothing of note on examination and her blood pressure was 132/70 mmHg. Other investigations on the clinical portal revealed a creatinine of 80 micromol/l (50-100), urea 5.5 mmol/l (3-8), normal FBC and PTH was 20.3 pmol/l (3-8) with a vitamin D of 70 nmol/l (>50). She had had a DEXA scan roughly one year ago with a nadir T score of –2.0.

Which of the following is the most appropriate approach to the management of this patient?

- **A)** No immediate treatment required and manage conservatively
- **B)** Refer for consideration of expedient parathyroid surgery
- **C)** Stop vitamin supplements and treat with oral bisphosphonates
- **D)** Treat with cinacalcet
- **E)** Treat with IV bisphosphonates and refer to surgical team

Answer

Correct answer : No immediate treatment required and manage conservatively

Explanation

This patient has mild primary hyperparathyroidism as revealed by the high calcium and raised PTH. The symptom of fatigue is probably unrelated. The vitamin D is fine. This patient can be conservatively managed according to the NIH criteria.

Reference

- Khan, A.A., Hanley, D.A., Rizzoli, R., Bollerslev, J., Young, J.E.M., Rejnmark, L., Thakker, R., D'Amour, P., Paul, T., Van Uum, S. and Shrayyef, M.Z., 2017. Primary hyperparathyroidism: review and recommendations on evaluation, diagnosis, and management. A Canadian and international consensus. Osteoporosis International, 28(1), pp.1-19.

Question 39

A 68-year-old postmenopausal woman is a known to have osteoporosis. However, she is not taking any anti-osteoporotic medication despite it being prescribed. She recently fell in her bathroom and has experienced back pain for the last 2-3 weeks. The pain is mild to moderate in its severity. An imaging of the spine confirms the presence of multiple compression fractures of the thoracolumbar vertebra. The patient has no neurological deficit as a result of the fracture. What is the best short-term management of the patient with regards to her pain apart from the advice on activity and physical therapy?

- **A)** Prescribe analgesics
- **B)** Prescribe analgesics with oral calcitriol for pain relief
- **C)** Prescribe analgesics with weekly alendronate tablets for pain relief
- **D)** Refer her to a spine surgeon for percutaneous balloon kyphoplasty
- **E)** Refer her to a spine surgeon for percutaneous vertebroplasty

Answer

Correct answer : Prescribe analgesics

Explanation:

The first line treatment for mild to moderately painful vertebral compression fracture associated with osteoporosis in post-menopausal women is the use of analgesics.

Calcitriol is a vitamin D analogue. The use of calcitriol for pain relief has not been proven. (Genev et al., 2017) Additionally, the use of calcitriol in patients in whom the PTH action is intact is not justified and can potentially increase the risk of iatrogenic hypercalcemia. (Balachandran, Asirvatham and Mahadevan, 2019)

Though injectable pamidronate has been found to help in pain relief in some studies, the role or oral bisphosphonate for pain relief has not been proven. Though bisphosphonates would be useful for this patient for long term osteoporosis management, the use of the oral agent for pain relief is not justified.(Genev et al., 2017)

Vertebral augmentation therapies in the form of percutaneous balloon Kyphoplasty or Percutaneous Vertebroplasty is reserved for those patients in whom pain continues after an acute unhealed vertebral fracture despite optimal pain management. It should NOT be used as first line therapy for pain relief in this situation. (Stevenson et al., 2014)

Reference:

- Balachandran, K., Asirvatham, A. R. and Mahadevan, S. (2019) 'Calcium–calcitriol: A match made in heaven?', Indian Journal of Endocrinology and Metabolism. Wolters Kluwer--Medknow Publications, 23(6), p. 649.
- Genev, I. K. et al. (2017) 'Spinal compression fracture management: a review of current treatment strategies and possible future avenues', Global spine journal. SAGE Publications Sage CA: Los Angeles, CA, 7(1), pp. 71–82.
- McCARTHY, J. and Davis, A. (2016) 'Diagnosis and management of vertebral compression fractures', American family physician, 94(1), pp. 44–50.
- Stevenson, M. et al. (2014) 'Percutaneous vertebroplasty and percutaneous balloon kyphoplasty for the treatment of osteoporotic vertebral fractures: a systematic review and cost-effectiveness analysis', in Percutaneous vertebroplasty and percutaneous balloon kyphoplasty for the treatment of osteoporotic vertebral fractures: a systematic review and cost-effectiveness analysis. NIHR Journals Library

Question 40

A 71-year-old man is admitted with cramps and twitching which have deteriorated over the last 2 weeks. He denies any change in bowel habit, and has a past history of type 2 diabetes and hypertension. He was taking metformin and recently started sitagliptin. He also takes bendrofluazide, ramipril and omeprazole for GORD.

On examination, trousseau's sign was positive, his pulse was 88bpm and blood pressure 128/88 mmHg.

His investigations revealed:

Sodium	142 mmol/l	(134-144)
Potassium	3.5 mmol/l	(3.5-5.5)
Urea	5.5 mmol/l	(3-8)
Creatinine	80 micromol/l	(50-100)
Calcium	1.80 mmol/l	(2.2-2.6)
Phosphate	0.8 mmol/l	(0.7-1.5)
PTH	5 pmol/l	(3.5-5.5)
HbA1c	55 mmol/mol	(<48)

Which of the following would you request?

- **A)** 1,25 diOH-vitamin D concentration
- **B)** 25-OH-Vitamin D concentration
- **C)** Calcitonin concentrations
- **D)** Magnesium concentration
- **E)** Urine calcium excretion

Answer

Correct answer : Magnesium concentration

Explanation

This patient has a low calcium and lowish phosphate, and a with a normal PTH concentration, which is rather inappropriate for this level of hypocalcaemia. This does suggest hypoparathyroidism, with the likely cause of this being hypomagnesaemia, probably due to PPI treatment. PPI therapy is associated with hypomagnesaemia due to inhibition of magnesium uptake in the small bowel. PPIs may also inhibit calcium uptake, but its effect is potentially more profound through inhibiting PTH release from parathyroid cells through interference with calcium sensing receptors.

The FDA released a warning regarding the potential impact of PPIs on hypomagnesaemia back in 2005.

Reference:

- Florentin, M. and Elisaf, M.S. (2012) Proton pump inhibitor-induced hypomagnesemia: A new challenge. World journal of nephrology, 1(6), p.151.

Question 41

A 22 year old boy is reviewed in clinic to investigate the cause of his low calcium levels. He is noticed to have short stature and shortened fourth and fifth metacarpals. The following are the blood results as checked in endocrinology clinic:

		Normal Ranges
Calcium	2.05 mmol/L	(2.2-2.6 mmol/L)
Phosphate	1.8 mmol/L	(0.8-1.5)
ALP	110 U/L	(50-125)
PTH	18 pmol/L	(1.0-6.1)

What is the likely diagnosis?

- **A)** McCune Albright syndrome
- **B)** Osteomalacia
- **C)** Paget's disease
- **D)** Pseudohypoparathyroidism
- **E)** Pseudo Pseudohypoparathyroidism

Answer

Correct answer : Pseudohypoparathyroidism

Pseudohypoparathyroidism (PHP) is a heterogeneous group of disorders characterized by low calcium, elevated phosphate levels and resistance to PTH activity. These individuals have short stature, round faces and shortened fourth metacarpals.

Question 42

A 65-year-old man with type 2 Diabetes mellitus and end stage renal disease was reviewed in an endocrine clinic after blood tests. He was on peritoneal dialysis for the last 3 months. He was vitally stable. There was a right paramedian placement of a peritoneal dialysis catheter. Blood studies reveal:

Urea	25.5mg/dL	(7-20)
Creatinine	390umol/L	(60-115)
Calcium (corrected)	2.25mmol/L	(2.2-2.6)
Phosphate	2.07mmol/L	(0.8-1.5)
Intact PTH	87pmol/L	(1-6)

According to NICE guidelines, in addition to phosphate binders administration, which drug is the most appropriate treatment?

- **A)** Alendronate
- **B)** Calcitonin
- **C)** Calcitriol
- **D)** Cinacalcet
- **E)** Elective parathyroidectomy

Answer

Correct answer : Cinacalcet

Explanation:

This patient's biochemistry is suggestive of secondary hyperparathyroidism in the setting of dialysis-dependent end-stage renal disease. Hyperphosphatemia, hypocalcaemia and deficiency of 1,25 dihydroxy vitamin D all stimulate PTH secretion. Oral calcium-containing phosphate binders (calcium acetate or calcium carbonate) or calcium-free phosphate binders (Sevelamer) prevent an increase of PTH secretion in CKD by preventing an increase in phosphate levels.

Cinacalcet is a calcimimetic agent directly modulating the calcium-sensing receptor in the parathyroid by increasing the receptor's sensitivity to extracellular calcium, thereby reducing the secretion of PTH. According to NICE guidelines, it is recommended for the treatment of secondary hyperparathyroidism in patients with end-stage renal disease only in those:

- Who have very uncontrolled levels of intact PTH (>85pmol/L) that are refractory to standard therapy and a normal adjusted serum calcium.
- Those in whom surgical parathyroidectomy is contraindicated because of the risks outweigh the benefits.

Both alendronate and calcitonin are antiresorptive agents that have only modest effects on calcium and phosphate levels. Neither drug would address this patient's underlying hyperparathyroidism. Although calcitriol is likely to decrease PTH levels, it can also increase calcium and phosphate levels. Given the strong association between Hyperphosphataemia and mortality, calcitriol should be avoided in this case. Surgical parathyroidectomy is not recommended in this case as perioperative risk is greater with renal failure than with normal renal function.

Reference:

- NICE (2007) NICE guideline [TA117]. Cinacalcet for the treatment of secondary Hyperparathyroidism in patients with end-stage renal disease in maintenance dialysis therapy.

Question 43

A 13-year-old boy was referred to the endocrine clinic for investigations due to his short stature. On examination, he had a round face with a short thick-set figure and brachydactyly. He was overweight with a BMI of 28kg/m^2. An X-ray of the right hand showed small subcutaneous ossified lesions.
Blood tests revealed:

Test	Result	Normal Range
Corrected Calcium	2.35mmol/L	(2.2-2.6)
Phosphate	1.2mmol/L	(0.8-1.5)
PTH	4.7pmol/L	(1.6-7.2)
TSH	3.1 mU/L	(0.35-5.5)

What is the most likely diagnosis based on the clinical features and biochemical profile?

- **A)** Osteoma cutis
- **B)** PHP1A like Acrodysostosis
- **C)** Pseudohypoparathyroidism type IA (PHP1A)
- **D)** Pseudohypoparathyroidism type IB (PHP1B)
- **E)** Pseudopseudohypoparathyroidism (PPHP)

Answer

Correct answer : Pseudopseudohypoparathyroidism (PPHP)

Explanation:

Pseudohypoparathyroidism (PHP) is a condition characterised by end-organ resistance to PTH resulting in increased serum PTH levels, hypocalcaemia and hyperphosphatemia. These patients have specific somatic and developmental abnormalities such as round face, short stature, obesity, subcutaneous ossifications (SCOs), brachydactyly (short metacarpals and metatarsals) and cognitive impairment.

PHP1A is associated with these biochemical and developmental abnormalities. However, some patients show the same physical features but normal calcium, phosphate and PTH levels are named as pseudopseudohypoparathyroidism (PPHP), as seen in this case. The physical phenotype of both PHP1A and PPHP is termed as Albright hereditary osteodystrophy (AHO). AHO is caused by inactivating mutations in the GNAS1 gene. Patients with PHP1A also show resistance to other hormones such as TSH, LH, FSH and GHRH, while patients with PPHP have AHO phenotype without other hormone resistance or severe obesity. Patients with PHP1B are overweight but have normal stature or mild brachydactyly and have biochemical abnormalities similar to PHP1A.

Other conditions in the PHP spectrum of disorder, including acrodysostosis syndrome, are similar to AHO but with a more severe skeletal phenotype including midfacial/nasal hypoplasia without subcutaneous ossifications (SCOs). SCOs is a striking feature of PHP1A and PPHP that can be painful, impair activities of daily living and occur over pressure areas. When occurring in isolation without other skeletal abnormalities of PHP, the condition is termed as osteoma cutis.

Reference:

- Germain-Lee, E.L., 2019. Management of pseudohypoparathyroidism. Current opinion in pediatrics, 31(4), p.537.

Question 44

A 56-year-old man presents in the endocrine clinic with complaints of polyuria, and polydipsia. He describes suffering from "off and on" constipation for the past 2 months. His systemic examination is unremarkable.
Blood tests reveal:

Test	Result	Normal Range
Urea	12.4mg/dL	(7-20)
Creatinine	105umol/L	(60-115)
Random glucose	136mg/dL	(<200)
HbA1c	5.6%	(<5.7%)
Corrected calcium	2.6mmol/L	(2.2-2.6)

According to NICE guidelines, what is the most appropriate next step?

- **A)** Consider a DXA (dual-energy X-ray absorptiometry) scan of spine
- **B)** Measure 24-hour urinary calcium excretion
- **C)** Measure ionised calcium
- **D)** Measure random PTH levels
- **E)** Repeat corrected (albumin adjusted) serum calcium

Answer

Correct answer : Repeat corrected (albumin adjusted) serum calcium

Explanation:

Primary hyperparathyroidism can present with any of the following features:

- symptoms of hypercalcemia, such as thirst, frequent or excessive urination or constipation
- osteoporosis or a previous fragility fracture
- a renal stone
- an incidental finding of elevated albumin-adjusted serum calcium (2.6 mmol/litre or above)
- NICE guidelines recommend measuring albumin-adjusted serum calcium for people with any of these features which might indicate primary hyperparathyroidism. Repeat the albumin-adjusted serum calcium measurement at least once if the first measurement is either:
- 2.6 mmol/litre or above or
- 2.5 mmol/litre or above and features of primary hyperparathyroidism are present
- NICE guidelines do not recommend measuring ionised calcium when testing for primary hyperparathyroidism. Measure parathyroid hormone (PTH) for people whose albumin-adjusted serum calcium level is either 2.6 mmol/litre or above on at least 2 separate occasions or 2.5 mmol/litre or above on at least 2 separate occasions and primary hyperparathyroidism is suspected. 24-hour urinary calcium excretion is used to differentiate primary hyperparathyroidism from familial hypocalciuric hypercalcaemia. For people with a confirmed diagnosis of primary hyperparathyroidism, further assessment is done by measuring eGFR (estimated glomerular filtration rate) or a DXA (dual-energy X-ray absorptiometry) scan of the lumbar spine, distal radius and hip and ultrasound scan of the renal tract.

Reference:

- NICE (2019) NICE guideline [NG132]. Hyperparathyroidism (primary): diagnosis assessment and initial management.

Question 45

A 6-year-old boy was brought to the endocrine clinic by his mother with complaints of poor weight gain. With regard to his developmental milestones, his speech and social and fine motor skills were appropriate for his age. The child's mother stated that he had delayed gross motor development, as at the age of 4 years he couldn’t sit without support or stand, which could be attributed to constant severe bone pain. His mother reported adequate nutritional intake. He had suffered with recurrent chest infections over the last year. On examination, his weight was 7 kg, he had normal hair distribution and had widening of the wrist and genu varus of lower limbs.
His blood tests revealed:

Test	Result	Normal Range
Urea	11mg/dL	(7-20)
Creatinine	102umol/L	(60-115)
Hb.	9.06gm/dL	(11-15)
Corrected calcium	2.02mmol/L	(2.2-2.6)
Phosphate	0.6mmol/L	(0.8-1.5)
Alkaline phosphatase	450IU/L	(50-110)
Serum PTH	12.2pmol/L	(1.3-7.6)
25OHD	90nmol/L	(25-125)
1,25(OH)2D	30pmol/L	(43-144)

An X-ray of his limbs showed a fracture of the mid-radius with significant cortical thinning. Which of the following is the most likely diagnosis consistent with this child's clinical and biochemical profile?

- **A)** Vitamin D deficiency
- **B)** Vitamin D-dependent rickets type I
- **C)** Vitamin D-dependent rickets type IIA
- **D)** Vitamin D-dependent rickets type IIB
- **E)** Vitamin D- resistant rickets (X-linked hypophosphataemia)

Answer

Correct answer : Vitamin D-dependent rickets type I

Explanation:

Vitamin D deficiency can present as osteomalacia or rickets. Osteomalacia occurs when there is inadequate mineralization of mature bone leading to a build-up of excessive unmineralised osteoid within the skeleton, while rickets is a disorder of the growing skeleton where there is inadequate mineralisation of bone as it is laid down at the epiphysis leading to a build-up of unmineralised osteoid in the growth plate. Patients can present with bone pain, deformity, fracture, proximal myopathy and children with growth retardation, bowing of long bones, widening of growth plates, wrists and rickety rosary. Biochemical abnormalities include, low calcium, phosphate, 25OHD and its active form 1, 25(OH)2D with raised ALP and PTH levels.
Rickets can be vitamin D dependent (VDDR) or vitamin D resistant. VDDR type I is due to congenital absence of 1 a-hydroxylase enzyme which is involved in conversion of vitamin D to its active form 1, 25(OH)2D in kidneys. It is inherited as autosomal recessive fashion and leads to profound rickets with myopathy and enamel hypoplasia. Biochemical abnormalities are similar to vitamin D deficiency apart from normal 25OHD with low 1,25(OH)2D. This patient's clinical features, biochemical profile and radiological findings are consistent with VDDR type I. Moreover, he had recurrent chest infections which can be explained by the fact that vitamin D is also important in both innate and adaptive immune response and anaemia that can be explained by the fact vitamin D has a vital role in promoting erythropoietin by downregulating proinflammatory cytokines and activating the erythropoietin hormone itself.
VDDR type II is due to a detective vitamin D receptor leading to vitamin D resistance. It is an autosomal recessive condition. In addition to the features of vitamin D deficiency, two-thirds of patients have total alopecia. If alopecia is present, it is often termed as type IIA in contrast to type IIB and type I where hair growth is normal. This patient had normal hair distribution. Biochemical abnormalities are similar to type I apart from raised 1,25(OH)2D.
Vitamin D-resistant rickets, or X-linked hypophosphataemia, is an X-linked dominant disorder that presents as severe rickets and osteomalacia along with short stature. Proximal myopathy is absent. Adults suffer from excessive new bone growth, particularly affecting entheses and longitudinal ligaments of the spinal canal. This can cause spinal cord compression which may need surgical decompression. These patients have normal calcium, vitamin D and PTH but low phosphate and high ALP levels.

Reference:

- Wass, J. and Owen, K. (2014) Oxford handbook of Endocrinology and Diabetes. 3rd edn.

Pakistan: Oxford University Press. (Book)

- Godfrey, E.K., Mussa, F., Kazahura, P., Shoo, A., Naburi, H. and Manji, K.P., 2020. Vitamin D-Resistant Rickets Diagnostics and Treatment Challenges at Muhimbili National Hospital, Tanzania. Case reports in endocrinology, 2020.

Question 46

This is the DEXA report on a 72-year-old female that has been seen privately as she is concerned regarding her risk of osteoporosis.

Region	BMD (g/cm^2)	T-Score	Z-Score
AP Spine (L1-L4)	1.016	-0.3	1.7
Femoral Neck (Left)	0.668	-1.6	0.0
Total Hip (Left)	0.816	-1.0	0.3
Femoral Neck (Right)	0.725	-1.1	0.5
Total Hip (Right)	0.834	-0.9	0.5
Femoral Neck Mean	0.696	-1.4	0.3
Total Hip Mean	0.825	-1.0	0.4

She has a family history of osteoporotic fracture, in that her mother had this condition in later life. She takes no medication currently and has no history of note. She went through the menopause at the age of 52.
How do you interpret this report with reference to the femoral neck?

- **A)** Normal bone mineral density
- **B)** Osteomalacia
- **C)** Osteopaenia
- **D)** Osteopetrosis
- **E)** Osteoporosis

Answer

Correct answer : Osteopaenia

Explanation:

This patient’s DEXA reveals T scores of less than -1 at the left and right femoral necks and the total hip reflecting osteopaenia (-1 to -2.4). Osteoporosis is reflected as a T score of -2.5 or below. In this patient’s case one should also refer to a FRAX but it would appear that pharmacological intervention would be unnecessary.

Reference:

- Interpretation of DEXA

Question 47

A 72-year-old female that has had a DEXA performed privately presents as she is concerned regarding her risk of osteoporosis. Her DEXA scan shows T-scores of between -0.5 to -1.4 in regions of hips and spine. She provides a history of her mother having quite bad osteoporosis later in life and she is rather fearful of this. Which of the following is the most appropriate step in the management of this patient?

- **A)** Calculate a FRAX before considering any treatment
- **B)** Reassure and discharge
- **C)** Recommend a weekly bisphosphonate
- **D)** Recommend denosumab
- **E)** Recommend HRT

Answer

Correct answer : Calculate a FRAX before considering any treatment

Explanation:

The correct answer is to calculate a FRAX score. When considering treatment a FRAX score will allow the determination of a 10 year risk for major osteoporotic risk fractures and therefore guide pharmacological intervention as per the NOGG guidance. This patient should of course receive guidance on lifestyle interventions such as calcium/vitamin D intake plus weight bearing exercise.

Reference:

- FRAX®Fracture Risk Assessment Tool

Question 48

A 72-year-old female that has had a DEXA performed privately presents as she is concerned regarding her risk of osteoporosis. Her DEXA scan shows T-scores of between -0.5 to -1.4 in regions of hips and spine. She provides a history of her mother having quite bad osteoporosis later in life and she is rather fearful of this. Which of the following is the most appropriate step in the management of this patient?

- **A)** Calculate a FRAX before considering any treatment
- **B)** Reassure and discharge
- **C)** Recommend a weekly bisphosphonate
- **D)** Recommend denosumab
- **E)** Recommend HRT

Answer

Correct answer : Calculate a FRAX before considering any treatment

Explanation:

The correct answer is to calculate a FRAX score. When considering treatment a FRAX score will allow the determination of a 10 year risk for major osteoporotic risk fractures and therefore guide pharmacological intervention as per the NOGG guidance. This patient should of course receive guidance on lifestyle interventions such as calcium/vitamin D intake plus weight bearing exercise.

Reference:

- FRAX®Fracture Risk Assessment Tool

Question 1

A 53 year old lady with a 3 year history of type 2 diabetes is reviewed in clinic; she has a previous history of hypothyroidism but has no other medical history of note. Her current medication includes metformin 500 mg three times a day, simvastatin 20 mg at night, ramipril 2.5 mg once a day and thyroxine 100 mcg once a day.

On examination her BMI is 32 kg /m^2 blood pressure 135/85 mmHg and her pulse is 62 beats per minute.

Investigations reveal:

		Normal Ranges
Hba1c	58.5 mmol/mol 7.5%	(<42.1 mmol/mol (6))
total cholesterol	6.3 mmol/l	(<5)
LDL-C	4.1 mmol/l	(<2)
triglyceride	2.1 mmol/l	(0.9 - 2.2)
eGFR	> 96 /min / 1.73 m^2	(90 - 110)
TSH	25 mu / l	(0.32 - 5.5)
Free T4	9.3 pmol/l	(9.3 - 23.4)

Which of the following is the most appropriate treatment option to optimise this lady's lipid profile?

- **A)** Add Fenofibrate
- **B)** Commence Atorvastatin
- **C)** Increase Simvastatin
- **D)** Increase Metformin
- **E)** Increase thyroxine

Answer

Correct answer : Increase thyroxine

This lady appears to have sub-optimal thyroid hormone replacement which is likely to contribute to her dyslipidaemia. Hypothyroidism is a recognised risk factor for lipid lowering therapy associated myotoxicity, therefore prior to escalating her specific lipid lowering medications it is important to correct her thyroid profile.

Question 2

A 42 year old South Asian gentleman is referred to the diabetic clinic by his GP. He has a 5 year history of type 2 diabetes. He complains of feeling tired and has a previous history of ischaemic heart disease.

On examination BMI 34 kg m^2, pulse 52 bpm, blood pressure 148/78 mmHg. Current medication consists of 'Novomix 30/70' mixed insulin - 42 IU twice daily, metformin 500 mg twice daily, simvastatin 20 mg od, aspirin 75 mg od, enalapril 20 mg od, atenolol 50 mg od.

Investigations

		Normal Ranges
Hbalc	62.8 mmol/mol (7.9%)	(42.1 mmol/mol <(6))
Total Cholesterol	6.9 mmol/l	(<5)
LDL-Cholesterol	4.5 mol/l	(< 3)
Triglyceride	2.9 mmol/l	(0.9 - 2.2)
U + Es	Normal	
TSH	32.8 mu / l	(0.3 - 5.5)
Free T4	6.9 pmol / l	(9.8 - 23.6)

Which of the following is the most appropriate approach to optimise this patient's lipid profile?

- **A)** Improve glycaemic control
- **B)** Commence thyroxine
- **C)** Commence fenofibrate
- **D)** Commence omega 3 fish oil
- **E)** Increase simvastatin dose

Answer

Correct answer : Commence thyroxine

This patient is hypothyroidic and correction of his thyroid status will also improve both his glucose control and lipid profile. Increasing the statin dose or commencing a fibrate is not appropriate as hypothyroidism is a risk factor for dyslipidaemia per se and is also associated with increased risk of myotoxicity with lipid-lowering therapies. Omega-3 fish oils are not routinely recommended for use in this setting.

Question 3

A 51 year old female with a ten year history of hypothyroidism takes thyroxine 100 micrograms daily. Previous thyroid function tests performed on an annual basis were normal, however a most recent thyroid function test reveals:

		Normal Ranges
Free T4	10.1 pmol/l	(9-22)
TSH	10.2 mu/l	(0.5-5)

Recently she has been treated for menopausal symptoms with female HRT and has also begun taking aspirin and simvastatin.
What is the likely cause for the change in her thyroid function?

- **A)** Aspirin
- **B)** Atrophic thyroiditis
- **C)** HRT
- **D)** Non-compliance
- **E)** Statin therapy

Answer

Correct answer : HRT

The likely cause for the change in TFTs is the addition of HRT which causes a rise in thyroid binding proteins and so would effectively reduce the free thyroid hormone concentrations requiring an increase in thyroxine dose.

TFTs with HRT

Question 4

A 21 year old male presents with a sudden onset weakness and is unable to move for approximately 1 hour. He gives little other history except for losing two to three pounds in weight over the last two months. On admission to hospital, he has a pulse of 100 bpm, a blood pressure of 105/80 mmHg but he has made a full recovery and muscle strength is normal with normal reflexes and flexor plantar responses. His investigations reveal:

		Normal Ranges
FBC	Normal	
U+Es	Normal	
LFTs	Normal	
Calcium	2.25 mmol/l	(2.2 - 2.6)
Glucose	5.5 mmol/l	(3.5 - 5.5)

Which of the following would be an appropriate investigation for this patient?

- **A)** 24hr Urine free cortisol
- **B)** EMG
- **C)** Oral glucose tolerance test
- **D)** Thyroid function tests
- **E)** Vitamin D concentration

Answer

Correct answer : Thyroid function tests

This young male presents with a sudden onset of complete weakness with speedy recovery. The diagnosis suggests hypokalaemic periodic paralysis and one finds that the potassium is low only during the episodes of weakness. However, a form fruste of this is thyrotoxic periodic paralysis and the patient should have TFTs assessed.

Question 5

A 24 year old female presents for annual thyroid function testing but complains of tiredness. She has been diagnosed with hypothyroidism 3 years ago and has been on thyroxine 100 micrograms daily. She also takes the OCP, microgynon for the last three years and over the last six months takes iron tablets due to iron deficiency anaemia. She claims to be compliant with therapy. Her TFTs have been quite stable over the last few years on the dose of thyroxine but her most recent TFT reveals:

		Normal Ranges
Free T4	8.8 pmol/l	(9-22)
TSH	12.1 mu/l	(0.5-5)

Which of the following is the likely explanation for her change in thyroid function?

- **A)** Atrophic thyroiditis
- **B)** Diverticulitis
- **C)** Iron tablets
- **D)** Non-compliance
- **E)** Oral contraceptive

Answer

Correct answer : Iron tablets

The patient’s TFTs have deteriorated since her last annual TFT and she now appears hypothyroidic despite assurance as to her compliance. The most likely explanation is the addition of iron tablets which reduce absorption of thyroxine. It should be explained to the patient that the thyroxine and iron should be taken separately. Non-compliance is unlikely and the use of the OCP co-exists with previous normal thyroid function. Coeliac disease is a less likely explanation for the iron deficiency anaemia and is not associated with reduced thyroxine absorption.

Question 6

In a study of 950 subjects with thyroid nodules, a new serological marker for thyroid carcinoma was assessed against formal histology. The following results were obtained:

		Normal Ranges
	Test positive	**Test Negative**
Histology Positive	40	10
Histology Negative	840	60

Which of the following describes the sensitivity of the new test?

- **A)** 40%
- **B)** 55%
- **C)** 66%
- **D)** 80%
- **E)** 95%

Answer

Correct answer : 80%

Sensitivity refers to the test's ability to correctly detect ill patients who do have the condition. In the example of a medical test used to identify a disease, the sensitivity of the test is the proportion of people who test positive for the disease among those who have the disease. Mathematically, this can be expressed as: sensitivity is true positive /true positives plus false negatives in this case 40/40 plus 10 equals to 80 %

Question 7

A 33 year old female presents with a 3 month history of agitation. On examination, she has a fine tremor of the out-stretched hands and lid lag. There is no palpable goitre. Her investigations reveal:

		Normal Ranges
Free T4	15.5 pmol/l	(9 - 23)
TSH	<0.02mu/l	(0.5 - 5)
Free T3	9.9 pmol/l	(3 - 6)
TSh Receptor Antibody	1.1 u/l	(<2)
TPO antibodies	105 u/l	(<140)

Which of the following would be the most appropriate investigation for this patient?

- **A)** Alpha-subunit concentration
- **B)** Assessment for mutations in TR-beta gene
- **C)** Radio-iodine uptake scan
- **D)** TRH stimulation test
- **E)** Ultrasound thyroid

Answer

Correct answer : Radio-iodine uptake scan

This patient has overt thyrotoxicosis with suppressed TSH but isolated elevation of T3. This is not thyroid hormone resistance. Whilst there is no palpable abnormality of the thyroid, the likelihood is that there is a functional adenoma, as both TPO and TSH receptor antibodies are negative. The most appropriate way of determining if there is a functional adenoma is through a radio-iodine uptake (RAI) uptake scan. An ultrasound of the thyroid really provides no useful information in this scenario.

Question 8

A 28 year old female presents with anxiety and tremor. On examination she has a pulse of 88 bpm, a fine tremor of the outstretched hands and a modest goitre with a faint bruit. There are no eye signs. Her investigations reveal:

		Normal Ranges
Free T4	38.9 pmol/l	(9 - 22)
TSH	2.1 mu/l	(0.5 - 5)
TSH receptor Antibody	1.1 mu/l	(<2)

An MRI of the pituitary reveals a 0.9 cm adenoma of the pituitary.
Which of the following would be the most appropriate initial treatment for this patient?

- **A)** Ablative radioactive iodine
- **B)** Carbimazole
- **C)** Pituitary surgery
- **D)** Radiotherapy
- **E)** Somatostatin analogue

Answer

Correct answer : Somatostatin analogue

This patient appears to have secondary thyrotoxicosis rather than thyroid hormone resistance as she is thyrotoxic with an abnormally 'normal' TSH. The patient would therefore require pituitary surgery but should first be rendered euthyroid as surgical/anaesthetic risk is higher in hyperthyroid cases. The most appropriate treatment prior to pituitary surgery would be restoration of euthyroidism and this can be achieved with somatostatin analogues. Radio-iodine would not be appropriate, as it is feasible that after surgery the patient would become euthyroid.

Question 9

A 22 year old female presents with tiredness and weight gain. She has a past history of childhood deafness and has been diagnosed with sensorineural deafness under the care of the ENT surgeons. On examination, she has a pulse of 64 bpm and a modest goitre is palpable. Her GP encloses the following blood results:

		Normal Ranges
Free T4	7.8 pmol/l	(9 - 23)
TSH	30 mu/l	(0.5 - 5)
TPO antibodies	180 u/l	(<140)

What is the most appropriate investigation for this patient?

- **A)** Alpha subunit measurement
- **B)** MRI pituitary
- **C)** PDS gene mutational analysis
- **D)** Perchlorate test
- **E)** TR-beta gene mutation analysis

Answer

Correct answer : PDS gene mutational analysis

The suggested diagnosis here is Pendred syndrome with a typical history of presentation in teens to early adulthood of primary hypothyroidism and early onset sensorineural deafness. The condition is autosomal recessive and associated with mutations of the PDS gene (SLC26A4) found on chromosome 7. SLC26A4 is a Iodide/Chloride cotransporter and defects in this lead to reduced organification of iodine and hence reduced uptake. The perchlorate test is seldom used in clinical practice being replaced by mutational analysis.

Question 10

A 32 year old female is referred by her GP as she had complained of a pain in the anterior aspect of her neck for a couple of months. The GP had arranged an ultrasound of the neck which revealed a 1.3 cm nodule of the left lobe of the thyroid and he had referred the patient to the thyroid clinic. There were no definite symptoms other than a vague complaint of discomfort in the throat which were probably anxiety related. Her weight had been steady and she was unaware of any lumps but had now been told that she had a lump in the thyroid by her GP and understandably was now more anxious and aware of a sticking feeling on swallowing. There are no abnormalities to note on examination of the neck and the patient appears clinically euthyroid. Investigations reveal:

		Normal Ranges
Free T4	14.5 pmol/l	(9 - 22)
TSH	2.4 mu/l	(0.5 - 5)
Thyroid Antibodies	negative	

What is the most appropriate course of action for this patient?

- **A)** Arrange FNA under ultrasound guidance
- **B)** Arrange radio-iodine uptake scan
- **C)** Reassure and discharge
- **D)** Refer for surgery
- **E)** Repeat ultrasound in 6 months

Answer

Correct answer : Arrange FNA under ultrasound guidance

This patient has a clinically inapparent thyroid nodule detected via ultrasound. The symptoms do not really tally with this lesion which would be clinically silent. However, one needs to establish if this lesion is benign or malignant and the first step should be a fine-needle aspiration (FNA) of the lesion under ultrasound guidance as one cannot clinically feel the lesion.

Reference

Management guidelines for patients with thyroid nodules and differentiated thyroid cancer

Question 11

A 22 year old male is referred to the endocrine clinic by the GP. He has a history of craniopharyngioma for which he takes full hormone replacement therapy including thyroxine 150 mg daily, hydrocortisone 10 mg bd and testosterone gel 60 mg daily. He is well, but his GP refers him to you as he is concerned by the attached thyroid function tests:

		Normal Ranges
Free T4	15.5 pmol/l	(9 - 22)
TSH	<0.02	(0.5 - 4.5)

There are no abnormalities to find on clinical examination of this patient.
Which of the following is the most appropriate action for this patient?

- **A)** Leave dose of thyroxine unchanged
- **B)** Reduce dose of thyroxine to 100 micrograms/d
- **C)** Reduce dose of thyroxine to 125 micrograms/d
- **D)** Request free T3 concentration
- **E)** Request TSH receptor antibodies

Answer

Correct answer : Leave dose of thyroxine unchanged

This is a frequent GP request. The important thing to recognise is that the patient is hypopituitary and so one cannot rely on TSH measurement. Therefore, the dose of thyroxine should be sufficient to aim for a thyroid hormone concentration in the mid to upper half of the normal range. This patient is stated to be well without any reported features of thyroid hormone excess – there is no need to measure free T3 and the dose of thyroxine should be left unchanged.

Question 12

A 22 year old male is referred by his GP with tiredness. Since the age of 5 he was treated for hypothyroidism and has had poor growth. He is currently receiving 100 micrograms of thyroxine daily. He is of short stature but has normal pubertal development. His investigations reveal:

		Normal Ranges
Free T4	14.6 pmol/l	(9 - 22)
TSH	0.5 mu/l	(0.5 - 5)
Testosterone	12.9 nmol/l	(9 - 30)
LH	2.8 mu/l	(2 - 10)
FSH	3.2 mu/l	(2 - 10)
IGF-1	5.2 nmol/l	(28 - 50)
Prolactin	33 mu/l	(50 - 450)
Cortisol post-synacthen	850 nmol/l	(>550)

CT of the head reports no abnormality of the pituitary.
What is the most appropriate investigation for this patient?

- **A)** Request KAL-1 mutational analysis
- **B)** Request MENIN mutational analysis
- **C)** Request MRI of the pituitary and olfactory bulbs
- **D)** Request Pit-1 mutational analysis
- **E)** Request SOX-1 mutational analysis

Answer

Correct answer : Request Pit-1 mutational analysis

It is rather unusual for a young child to have developed primary hypothyroidism and what is more this adult is now short with a low IGF-1 suggesting GH deficiency and a low prolactin suggesting hypoprolactinaemia. This would suggest a combined partial hypopituitarism - TSH, PRL and GH typical of a mutation of the transcriptional activator - pit-1. Prop-1 mutations (Prophet of Pit-1) are the most common defects in combined childhood pituitary hormone deficiencies and are characterised by LH/FSH deficiency together with GH, TSH and Prolactin. Later, ACTH deficiency may ensue. Imaging may reveal a small or indeed normal appearance of the pituitary and will tell us nothing of the functionality.

Question 13

A 24 year old female has received a twelve month course of carbimazole for Graves disease. She is a non-smoker, with no family history of thyroid dysfunction. She recently stopped treatment and attends two months later for subsequent review and complains of recurrence of her previous symptoms. On examination, she has a modest goitre with pulse of 80 bpm and has a fine tremor of the outstretched hands. There are no eye signs associated with Graves disease. The results of her thyroid function tests reveal:

		Normal Ranges
Free T4	32.3 pmol/l	(9 - 22)
TSH	<0.02	mu/l (0.5 - 5)

She informs you that she is keen on getting pregnant after about 6 months time (as she is due to get married in the summer). She is currently taking the oral contraceptive, microgynon. Which of the following would be the most appropriate action for this patient?

- **A)** Continue with further six months propylthiouracil
- **B)** Continue with long term propylthiouracil
- **C)** Continue to treat with long term carbimazole
- **D)** Radioactive iodine
- **E)** Refer for thyroid surgery

Answer

Correct answer : Radioactive iodine

The most appropriate first line treatment for this patient who has recurrent thyrotoxicosis following antithyroid treatment would be radioactive iodine. She should ensure that she does not become pregnant for six months after treatment but she is already taking the OCP. There is no report of eye disease associated with the Graves' so concomitant steroids is probably unnecessary. Following radioiodine treatment, approximately 80% of patients become hypothyroid.

Question 14

A 28 year old female who is one month postpartum develops tiredness. Thyroid function tests reveal:

		Normal Ranges
Free T4	25.6 pmol/l	(9 - 22)
TSH	<0.02 mu/l	(0.5 - 5)
TPO antibodies	550 iu/l	(<140)

When she is seen 2 months later she is still tired and emotionally labile. The results of TFTs reveal:

		Normal Ranges
Free T4	8.5 pmol/l	(9 - 22)
TSH	12 mu/l	(0.5 - 5)

She is treated with thyroxine 50 micrograms daily and her thyroid function tests improve. She is reviewed regularly and you see her one year later where she is well and has with the following thyroid function tests:

		Normal Ranges
Free T4	21.5 pmol/l	(9 - 22)
TSH	0.3 mu/l	(0.5 - 5)

Which of the following is the most appropriate action for this patient?

- **A)** Continue thyroxine in current dose
- **B)** Increase dose of thyroxine by 25 micrograms
- **C)** Reduce dose of thyroxine in 25 microgram increments
- **D)** Stop thyroxine and arrange radio-iodine uptake scan
- **E)** Stop thyroxine and reassess thyroid function

Answer

Correct answer : Stop thyroxine and reassess thyroid function

This patient is likely to have postpartum thyroiditis as suggested by the initial hyperthyroidism with subsequent hypothyroidism occurring postpartum. Approximately 30% have persistent hypothyroidism but the majority recover. There is a strong chance of further thyroid dysfunction in subsequent pregnancies. The most appropriate approach therefore, is to stop thyroxine and reassess thyroid function in approximately one month.

Question 15

A 21 year old male is admitted with a one hour history of profound muscle weakness such that he was immobile and unable to move his arms or legs. He was otherwise well, had noted some weight loss of late but denied use of illicit substances. He had one similar episode two months ago from which he recovered fully.

On admission, his BMI was 21 kg/m^2 , his pulse was 102 bpm, blood pressure was 112/80 mmHg and he had full muscle strength. Investigations reveal:

U+Es	Normal

Which of the following would be the most appropriate next investigation for this patient?

- **A)** Muscle biopsy
- **B)** Oral glucose tolerance test
- **C)** Thyroid function tests
- **D)** Urine catecholamines
- **E)** Urine free cortisol measurement

Answer

Correct answer : Thyroid function tests

This patient appears to have developed episodic and profound muscle weakness. The potassium is normal on admission but the patient has recovered fully. The history is compatible with hypokalemic periodic paralysis yet the tachycardia and recent weight loss is quite compatible with thyrotoxicosis. Therefore, a diagnosis of thyrotoxic periodic paralysis should be considered. During attacks, hypokalaemia typically occurs and the condition is best treated with restoration of euthyroidism.

Question 16

. A 35 year old female presented with a three month history of 3 kg weight loss and anxiety. On examination, she had mild tremors of the outstretched hands, proptosis and lid lag. Examination of the neck reveals an asymmetrically enlarged goitre with a 3.5 cm irregular nodule palpable in the left lobe. Investigations reveal:

		Normal Ranges
Free T4	24 pmol/l (9-23)	
TSH	<0.22 mu/l	(0.5-5)
TPO antibodies	>1500 mu/l	(<150)
TSH-R antibodies	3.3 iu/l	(<1)
Calcium	2.65 mmol/l	(2.2 -2.6)
U+Es	Normal	

The patient was initiated on carbimazole therapy.
Which of the following is the definitive diagnostic investigation to get the diagnosis for this patient?

- **A)** Thyroidectomy
- **B)** Fineneedle aspiration
- **C)** PTH concentration
- **D)** RET proto-oncogene
- **E)** Radio-iodine uptake scan

Answer

Correct answer : Fineneedle aspiration

This woman has Graves' disease and also has a left sided discrete nodule. In any nodule one should consider the possibility of a carcinoma and the most appropriate initial investigation would be a fine-needle aspiration (FNA) which would be diagnostic. This is not likely to be a toxic adenoma as the patient has positive TSH receptor antibodies indicating Graves’ disease. Therefore, radioiodine uptake scan would merely reveal increased uptake and the nodule may be cold or hot - this procedure would not be diagnostic. Ultrasound would add little diagnostic information. The slight elevation of calcium is not unusual in thyrotoxicosis.

Question 17

A 45 year old woman is referred by her GP for investigation of her hypercalcaemia. He noted the following investigations:

		Normal Ranges
U+Es	Normal	
Calcium	2.8 mmol/l	(2.2 - 2.6)
Phosphate	1.0 mmol/l	(0.8 - 1.4)

The patient originally attended the GP with vague aches and pains which have been present for two months or so and she also admits to feeling rather depressed. She is only taking fluoxetine 20 mg daily at present. There is nil of note on examination. Further investigations reveal:

		Normal Ranges
PTH	4.4 pmol/l	(3 - 5)
Vitamin D	55 nmol/l	(>50)
Urine calcium	7 mmol/d	(0 - 7.5)

Which of the following is the likely diagnosis?

- **A)** Drug-induced
- **B)** Familial hypocalciuric hypercalcaemia
- **C)** Milk-Alkali syndrome
- **D)** Primary hyperparathyroidism
- **E)** Tertiary hyperparathyroidism

Answer

Correct answer : Primary hyperparathyroidism

This patient has mild hypercalcaemia, an inappropriately normal PTH concentration and has a normal/highish urine calcium excretion. The latter would argue against a diagnosis of FHH where urine calcium excretion is low (less than 5 mmol/d) and so the likely diagnosis is primary hyperparathyroidism.

Question 18

A 32 year old female presents with a six month history of weight loss and anxiety. She does not report any visual symptoms and her visual acuity is normal. She is diagnosed with Graves' disease based on confirmatory thyroid function tests and a positive TSH receptor antibody. She is treated with carbimazole and thyroxine in a block and replacement regime for approximately six months. Treatment is then stopped. She re-attends clinic three months after stopping treatment and complains of once again feeling rather anxious and having poor sleep. She is a non-smoker and drinks little alcohol.
On examination, she has a fine tremor of the outstretched hands, lid lag and a goitre. Her thyroid function tests reveal:

		Normal Ranges
Free T4	38.2 pmol/l	(9 - 23)
TSH	<0.05 mu/l	(0.5 - 5)

She elects to have radio-iodine treatment. Which of the following concerning treatment with steroids would you elect?

- **A)** Commence treatment with prednisolone 20 mg daily on day of radio-iodine
- **B)** Commence treatment with prednisolone 40 mg daily on day of radio-iodine
- **C)** Commence treatment with prednisolone 40 mg daily, 1 week following radioiodine
- **D)** Commence treatment with prednisolone 40 mg daily, 1 week before radio-iodine
- **E)** No requirement to pre-treat with steroids

Answer

Correct answer : No requirement to pre-treat with steroids

In this patient, there does not appear to be any reported evidence of active Graves' Ophthalmopathy, in which case there is no need to pre-treat with steroids. If this patient had evidence of GO, then there is a 15% risk of deterioration of GO following RAI. This risk may be minimised by pre-treatment with prednisolone (0.5 mg/kg/d) continuing for 1 month then tapering down over the following month.

Question 19

A 42 year old female is seen due to anxiety and weight loss. She is found to have Graves' disease with positive TSH receptor antibodies. The physician elects to treat her with a block and replacement regime consisting of carbimazole and thyroxine for six months. He explains at that stage treatment will be withdrawn and thyroid function tests monitored for relapse. The patient enquires as to what are the chances of relapse after this treatment.
Which of the following most accurately reflects the relapse rate after treatment with antithyroid drugs?

- **A)** 10%
- **B)** 20%
- **C)** 30%
- **D)** 50%
- **E)** 70%

Answer

Correct answer : 50%

This is a relatively standard approach to the treatment of Graves' disease - give a block and replace regime for between 6-12 months. Studies suggest that this approach is associated with an approximate 50% long term remission rate.

Question 20

A 35 year old female with Graves' disease is treated carbimazole and relapses after treatment is withdrawn. Consequently, she elects to receive radio-iodine but after this treatment develops some grittiness and irritation of the eyes. Which of the following in this case may have contributed to the development of Graves' Ophthalmopathy?

- **A)** Consumption of approximately 22 units of alcohol weekly
- **B)** Myopia
- **C)** Previous treatment with thionamides
- **D)** Smoker of 10 cigarettes per day
- **E)** Use of the oral contraceptive

Answer

Correct answer : Smoker of 10 cigarettes per day

Factors recognised to contribute to the development/deterioration of Graves' Ophthalmopathy include smoking, rise in TSH and undertreatment of hypothyroidism together with high TSH receptor antibodies.

Question 21

A 45 year old female is referred by her GP with deranged thyroid function tests. She has been complaining of occasional palpitations hence her GP checked investigations and found the following:

		Normal Ranges
Free T4	16.5 pmol/l	
TSH	<0.05 mu/l	(0.5-5)
TPO Antibodies	100 iu/l	(<300)
TSH Receptor Antibody	0.2 iu/l	(<1.5)

There is nothing of note on examination with no palpable thyroid goitre.
Which of the following would be the most appropriate investigation for this patient?

- **A)** Request alternative TFT assay at another centre
- **B)** Thyroid FNA
- **C)** Thyroid microsomal antibodies
- **D)** Thyroid ultrasound
- **E)** Thyroid uptake scan

Answer

Correct answer : Thyroid uptake scan

This patient has subclinical hyperthyroidism and this is most likely due to a toxic impalpable adenoma. The most appropriate investigation would be a thyroid uptake scan which may be expected to reveal the toxic adenoma. Then, treatment with radio-iodine would be appropriate.

Question 22

A 55 year old female presents with a three week history of confusion. She has otherwise been well. Three years ago she was diagnosed with hypothyroidism for which she takes thyroxine 100 micrograms per day. On examination, she appears euthyroid but is confused, with inappropriate answers to questions and strange affect. CVS, respiratory and abdominal examination are all normal with a blood pressure of 126/78 mmHg.
Investigations including CSF examination, Head CT and MRI together with U+Es, Calcium and LFTs are all normal.

		Normal Ranges
Free T4	15.6 nmol/l	(9-22)
TSH	5.6 mu/l	(0.5-5)
TPO antibodies	>1500 mu/l	(<150)
Random cortisol	330 nmol/	(200-800)
LH	33 mu/l	(>10)
FSH	55 iu/l	(>10)

Which of the following is the likely diagnosis?

- **A)** Hashimoto's encephalopathy
- **B)** Lymphocytic hypophysitis
- **C)** Limbic encephalomyelitis
- **D)** MELAS
- **E)** POEMS

Answer

Correct answer : Hashimoto's encephalopathy

This patient has a short history of confusion yet the neurological investigations are normal. The likely diagnosis is therefore Hashimoto's encephalopathy considered to be part of an autoimmune encephalitis. The condition was described in the 1960s by a Professor Brain! The condition can be progressive or relapsing remitting and the treatment is steroids. Often, the condition presents prior to the development of hypothyroidism and patients can be entirely euthyroid yet with quite profound neurological dysfunction.

Question 23

A 70 year old male presents with a two month history of tiredness and lethargy. Six months ago he was treated for paroxysmal atrial fibrillation with amiodarone 200 mg daily.
On examination, he appeared to be euthyroid with no goitre palpable.
Investigations revealed:

		Normal Ranges
Serum free T4	26.2 pmol/L	(9-23)
Serum total T3	0.8 nmol/L	(3-5.5)
Serum TSH	9 mU/L	(0.5-5)

Which of the following is the likely diagnosis?

- **A)** Amiodarone-induced thyroid dysfunction
- **B)** Amiodarone induced thyrotoxicosis
- **C)** Hashimoto's hypothyroidism
- **D)** Sick euthyroid syndrome
- **E)** TSH secreting pituitary adenoma

Answer

Correct answer : Amiodarone-induced thyroid dysfunction

The results show increased T4, low T3 but elevated TSH, indicating hypothyroidism. This suggests amiodarone induced hypothyroidism which inhibits the peripheral conversion of T4 to T3.

Thyroid and Amiodarone

Question 24

A 32 year old male is diagnosed with Pendred's syndrome. Which of the following is typically found in Pendred's syndrome

- **A)** Cataract
- **B)** Mental retardation
- **C)** Optic atrophy
- **D)** Sensorineural deafness
- **E)** Thyroid agenesis

Answer

Correct answer : Sensorineural deafness

Pendred syndrome is an autosomal recessively inherited condition characterised by deafness, goitre, hypothyroidism and is due to defective iodine binding.

Question 25

A 32 year old female undergoes a radio-iodine uptake scan and this is reported to show 'generalised reduced uptake of 123I tracer throughout the thyroid'. In which of the following would this result be expected?

- **A)** De Quervain's thyroiditis
- **B)** Graves' disease
- **C)** Multi-nodular toxic goitre
- **D)** Thyroid nodule with papillary thyroid cancer
- **E)** Type 1 amiodarone induced thyrotoxicosis type 1

Answer

Correct answer : De Quervain's thyroiditis

De Quervain's thyroiditis is typically associated with a generalised low or absent 123I tracer uptake. The others will have high or normal uptake. In particular type 1 amiodarone-induced thyrotoxicosis may be distinguished from the thyroiditis of type 2 by the normal or high uptake scan.

Question 26

A 56-year-old woman presents with thyrotoxicosis. Examination reveals an enlarged thyroid with multiple nodules, confirmed on ultrasound scanning. Treatment with radioactive iodine is planned.

Which of the following is the recommended dose of radioiodine suggested for this patient?

- **A)** 50-100 MBq
- **B)** 200-400 MBq
- **C)** 500-800 MBq
- **D)** 900-1100 MBq
- **E)** 1200-1500 MBq

Answer

Correct answer : 500-800 MBq

The recommended dose of RAI is typically between 500 - 800 MBq with the frequent dose being 555 MBq.

Question 27

A 68 year old female presents with recurrent Graves' disease after having received one course of block and replacement therapy with carbimazole and thyroxine. After discussion, she elects to receive radioiodine treatment (RAI). Prior to receiving treatment she is rendered euthyroid again with carbimazole. At least how many days prior to her radioactive iodine should she stop her carbimazole?

- **A)** 7 days
- **B)** 14 days
- **C)** 21 days
- **D)** 28 days
- **E)** No requirement to stop carbimazole

Answer

Correct answer : 7 days

Carbimazole needs to be stopped at least 7 days prior to radioiodine to ensure appropriate uptake. The treatment is often used in patients who need to be rendered euthyroid prior to RAI due to the risk of early deterioration of thyrotoxicosis.

Question 28

A 35 year old female is referred with a left lower thyroid nodule that she inadvertently noticed whilst putting on a necklace. Examination reveals a 2 cm firm, mobile, non-tender nodule without any lymphadenopathy.

A fine-needle aspiration was performed in clinic and was reported as:

- 'Insufficient sample. Non-diagnostic or inadequate'.

Into which of the following classifications does this fit?

- **A)** Thy 1
- **B)** Thy 2
- **C)** Thy 3
- **D)** Thy 4
- **E)** Thy 5

Answer

Correct answer : Thy 1

The classification of thyroid biopsy samples is based uponfive criteria:

Thy 1:	insufficient sample or unable to report due to heavy blood staining.
Thy 2:	Non-neoplastic; normal thyroid, thyroiditis, colloid
Thy 3:	Neoplasm possible; samples suggesting follicular neoplasm
Thy4:	Suspicious of malignancy
Thy5:	Malignancy - confidence in diagnosing a malignancy with malignant cells seen

Question 29

A 28 year old female undergoes an fine-needle aspiration of an isolated 2cm thyroid nodule. This is reported as 'non-neoplastic suggestive of thyroiditis'.

Which of the following is the correct classification of this report?

- **A)** Thy 1
- **B)** Thy 2
- **C)** Thy 3
- **D)** Thy 4
- **E)** Thy 5

Answer

Correct answer : Thy 2

The classification of thyroid biopsy samples is based upon five criteria:

Thy 1:	Insufficient sample or unable to report due to heavy blood staining.
Thy 2:	Non-neoplastic; normal thyroid, thyroiditis, colloid
Thy 3:	Neoplasm possible; 3a - Atypia 3b- suspected follicular neoplasm
Thy4:	Suspicious of malignancy
Thy5:	Malignancy - confidence in diagnosing a malignancy with malignant cells seen

In this case, the cytology reports a thyroiditis - benign THY2.

Question 30

A 28 year old female undergoes a fine-needle aspiration of an isolated 2cm thyroid nodule.

This is reported as: 'a follicular neoplasm'.

Which of the following is the correct classification of this report?

- **A)** Thy 1
- **B)** Thy 2
- **C)** Thy 3
- **D)** Thy 4
- **E)** Thy 5

Answer

Correct answer : Thy 3

The classification of thyroid biopsy samples is based upon five criteria:

Thy 1:	Insufficient sample or unable to report due to heavy blood staining.
Thy 2:	Non-neoplastic; normal thyroid, thyroiditis, colloid.
Thy 3:	Neoplasm possible; samples suggesting follicular neoplasm.
Thy4:	Suspicious of malignancy.
Thy5:	Malignancy - confidence in diagnosing a malignancy with malignant cells seen.

In this case, the cytology reports a follicular neoplasm - suspicious THY3.

Question 31

A 28 year old female undergoes a fine-needle aspiration of an isolated 2cm thyroid nodule. This is reported as 'abnormal cells, suspicious of malignancy'.

Which of the following is the correct classification of this report?

- **A)** Thy 1
- **B)** Thy 2
- **C)** Thy 3
- **D)** Thy 4
- **E)** Thy 5

Answer

Correct answer : Thy 4

The classification of thyroid biopsy samples is based upon five criteria

Thy 1:	insufficient sample or unable to report due to heavy blood staining.
Thy 2:	Non-neoplastic; normal thyroid, thyroiditis, colloid
Thy 3:	Neoplasm possible; samples suggesting follicular neoplasm
Thy4:	Suspicious of malignancy
Thy5:	Malignancy - confidence in diagnosing a malignancy with malignant cells seen

In this case the suspicion of malignancy on the report indicates THY4

Question 32

A 28 year old female undergoes a fine-needle aspiration of an isolated 2cm thyroid nodule. This is reported as: 'diagnostic of malignancy'.

Which of the following is the correct classification of this report?

- **A)** Thy 1
- **B)** Thy 2
- **C)** Thy 3
- **D)** Thy 4
- **E)** Thy 5

Answer

Correct answer : Thy 5

The classification of thyroid biopsy samples is based upon five criteria:

Thy 1:	Insufficient sample or unable to report due to heavy blood staining.
Thy 2:	Non-neoplastic; normal thyroid, thyroiditis, colloid
Thy 3:	Neoplasm possible; samples suggesting follicular neoplasm
Thy4:	Suspicious of malignancy
Thy5:	Malignancy - confidence in diagnosing a malignancy with malignant cells seen

In this case the sample is diagnostic of malignancy indicating THY5

Question 33

A 28 year old female undergoes a fine-needle aspiration of an isolated 2cm thyroid nodule. This is reported as THY5.

Which of the following is the correct classification of this report?

- **A)** Abnormal, suspicious (but not diagnostic of) malignancy
- **B)** Diagnostic of malignancy
- **C)** Follicular lesions
- **D)** Non-diagnostic or inadequate
- **E)** Non-neoplastic (consistent with nodular goitre or thyroiditis)

Answer

Correct answer : Diagnostic of malignancy

The classification of thyroid biopsy samples is based upon five criteria

Thy 1:	Insufficient sample or unable to report due to heavy blood staining.
Thy 2:	Non-neoplastic; normal thyroid, thyroiditis, colloid.
Thy 3:	Neoplasm possible; samples suggesting follicular neoplasm.
Thy4:	Suspicious of malignancy.
Thy5:	Malignancy - confidence in diagnosing a malignancy with malignant cells seen.

Question 34

A 28 year old female undergoes an fine-needle aspiration of an isolated 2cm thyroid nodule. This is reported as THY4.

Which of the following is the correct interpretation of THY4?

- **A)** Abnormal, suspicious (but not diagnostic of) malignancy
- **B)** Diagnostic of malignancy
- **C)** Follicular lesions
- **D)** Non-diagnostic or inadequate
- **E)** Non-neoplastic (consistent with nodular goitre or thyroiditis)

Answer

Correct answer : Abnormal, suspicious (but not diagnostic of) malignancy

The classification of thyroid biopsy samples is based upon five criteria

Thy 1:	Insufficient sample or unable to report due to heavy blood staining.
Thy 2:	Non-neoplastic; normal thyroid, thyroiditis, colloid.
Thy 3:	Neoplasm possible; samples suggesting follicular neoplasm.
Thy4:	Suspicious of malignancy.
Thy5:	Malignancy - confidence in diagnosing a malignancy with malignant cells seen.

In this case the suspicion of malignancy on the report indicates THY4

Question 35

A 28 year old female undergoes an fine-needle aspiration of an isolated 2cm thyroid nodule. This is reported as THY3.

Which of the following is the correct interpretation of this report?

- **A)** Abnormal, suspicious (but not diagnostic of) malignancy
- **B)** Diagnostic of malignancy
- **C)** Follicular lesions
- **D)** Non-diagnostic or inadequate
- **E)** Non-neoplastic (consistent with nodular goitre or thyroiditis)

Answer

Correct answer : Follicular lesions

The classification of thyroid biopsy samples is based upon five criteria

Thy 1:	Insufficient sample or unable to report due to heavy blood staining.
Thy 2:	Non-neoplastic; normal thyroid, thyroiditis, colloid.
Thy 3:	Neoplasm possible; samples suggesting follicular neoplasm.
Thy4:	Suspicious of malignancy.
Thy5:	Malignancy - confidence in diagnosing a malignancy with malignant cells seen.

In this case follicular neoplasm indicates THY3

Question 36

A 76 year old lady presents with an enlarged thyroid gland with retrosternal extension. She is otherwise well in herself and clinically and biochemically euthyroid.

What is the next best investigation for further management of this lady?

- **A)** Endoscopy (upper GI)
- **B)** Flow volume loop
- **C)** Fine-needle aspiration cytology
- **D)** Radioiodine uptake
- **E)** Ultrasound neck

Answer

Correct answer : Flow volume loop

The thyroid gland is normally located beneath the cricoid cartilage midway between the apex of thyroid cartilage and the supra-sternal notch. It normally weighs about 10-20 g. The growth of the thyroid gland usually occurs in a downward and posterior direction as the anterior/ upward growth of the gland is limited by attachment of sterno-thyroid muscle to the thyroid cartilage. As a result an enlarging thyroid gland can expand and grow in retrosternal space compressing the surrounding structures like the trachea and oesophagus.

An inspiratory stridor is an indicator of compression of trachea and should be investigated by flow loop volume as it provides physiological evidence of obstruction. An ultrasound of the thyroid gland is a useful modality for detection of thyroid nodules and can help differentiate cystic from solid nodules but it is not a sensitive investigation to detect retrosternal gland extension and not employed routinely for evaluation of patients with goitre. CT imaging is also helpful to evaluate the retrosternal growth of thyroid gland and usually employed pre-operatively. The following are some of the keys points regarding surgical management of goitre:

- Patients with physiological evidence of airway obstruction (on flow volume loop) should have thyroidectomy (if they are fit for operation).
- Any hint of malignancy is an indication for surgical resection of the gland
- Elderly patients with a stable retrosternal goitre (with no significant symptoms and signs of tracheal/esophageal compression), should be managed conservatively. Follow up for such patients should include serial flow volume loops to assess for any airway compromise or serial CT thyroid/thorax to assess for any change in the size of the gland.

Question 37

A 76 year old lady presents with enlarged thyroid gland with an retrosternal extension. It is leading to inspiratory stridor. She is otherwise well in herself and is clinically/biochemically euthyroid. What is the most appropriate step in her management?

- **A)** Fine-needle aspiration cytology
- **B)** Observation
- **C)** Radioiodine ablation
- **D)** Thyroidectomy
- **E)** Thyroxine (low dose)

Answer

Correct answer : Thyroidectomy

The thyroid gland is normally located beneath the cricoid cartilage midway between the apex of thyroid cartilage and the supra-sternal notch. It normally weighs about 10-20 g. The growth of the thyroid gland usually occurs in a downward and posterior direction as the anterior/ upward growth of the gland is limited by attachment of sterno-thyroid muscle to the thyroid cartilage.

As a result, an enlarging thyroid gland can expand and grow in retrosternal space compressing the surrounding structures like the trachea and oesophagus. An inspiratory stridor is an indicator of compression of the trachea and should be investigated by flow loop volume as it provides physiological evidence of obstruction. An ultrasound of the thyroid gland is a useful modality for detection of thyroid nodules and can help differentiate cystic from solid nodules but it is not a sensitive investigation to detect retrosternal gland extension and not employed routinely for evaluation of patients with goitre. CT imaging is also helpful to evaluate the retrosternal growth of the thyroid gland and usually employed pre-operatively. The following are some of the keys points regarding surgical management of goitre:

- Patients with physiological evidence of airway obstruction (on flow volume loop) should have thyroidectomy (if they are fit for operation).
- Any hint of malignancy is an indication for surgical resection of the gland
- Elderly patients with a stable retrosternal goitre (with no significant symptoms and signs of tracheal/esophageal compression), should be managed conservatively. Follow up for such patients should include serial flow volume loops to assess for any airway compromise or serial CT thyroid/thorax to assess for any change in the size of the gland.

Question 38

A 17 year old with a background history of medullary thyroid carcinoma (MTC) which was previously treated with surgical resection, presents with a solitary cervical lymph node which on fine-needle aspiration cytology (FNAC) shows features of metastasis from the MTC. What is the most appropriate step in her management?

- **A)** External beam radiotherapy
- **B)** Octreotide
- **C)** Radical neck dissection
- **D)** Radioiodine ablation
- **E)** Suppressive dose of thyroxine

Answer

Correct answer : Radical neck dissection

The following points sum up the guidelines from the British Thyroid Association regarding the management of medullary thyroid cancer (MTC):

- The initial evaluation of suspected MTC patients should include FNAC and plasma calcitonin measurement.
- All patients (and affected families) should be offered clinical genetics service and *RET* gene testing.
- *RET* mutation testing should include screening of exons 10, 11, 13, 14, 15 and 16.
- Patients with MTC should be screened for MEN 2A and 2B
- Screen for pheochromocytomas and primary hyperparathyroidism by measuring 24 hour urinary catecholamine/ metanephrines and measurement of serum calcium respectively.
- Patients with MTC should undergo total thyroidectomy and level 6 lymph node dissection
- Prophylactic surgery should be offered in disease-free carriers of germline *RET* mutation. Surgery should be performed before the age of 5 years for MEN 2A patients and by the age of 1 year in MEN 2B patients.
- Patients should be monitored lifelong with monitoring of calcitonin levels.

Question 39

A 44 year old with previous history of papillary thyroid cancer (3 cm nodule), treated with total thyroidectomy and central lymph node dissection, presents for a regular annual review. Post-operatively she had received radioiodine ablation and has been asymptomatic leading up to the clinic visit. The blood tests done during the review reveal elevated thyroglobulin (Tg) levels, which were previously normal, and suppressed TSH < 0.01 (on thyroxine 200mcg daily). Her thyroglobulin antibodies are negative and an ultrasound of the neck plus whole body scan are negative. Which of the following is the most appropriate next step in her management?

- **A)** Decrease thyroxine dose
- **B)** PET scan
- **C)** Radio-iodine ablation
- **D)** Repeat Thyroglobulin levels in 3 months
- **E)** Surgical exploration

Answer

Correct answer : PET scan

Thyroglobulin (Tg) is a useful tumour marker, secreted by normal as well as cancerous thyroid cells. After complete thyroidectomy and postoperative radio-ablative therapy of a differentiated thyroid cancer (papillary or follicular), the Tg levels are usually undetectable. A detectable Tg level, such as in this scenario, is indicative of the presence of thyroid remnants or recurrence of the tumour.

Presence of endogenous Thyroglobulin antibodies may also interfere with the assay and so should be excluded by its simultaneous measurement.

In patients with rising or detectable Tg levels the following points should be kept in mind:

- Check Tg heterophile antibody levels to rule out interference in assay
- Check if the TSH is completely suppressed
- Did the patient undergo complete surgical resection
- Rule out any possible iodine contamination (e.g. amiodarone therapy or recent contrast injection) in cases where Tg is detectable and uptake scan negative
- Arrange a neck ultrasound to look for any thyroid remnant or lymph node enlargement
- If neck ultrasound negative arrange for CT thorax
- If both the above mentioned investigations are negative arrange for a ^{99}mTc MIBI to rule out bony deposits
- If all above mentioned investigations are negative consider a PET scan, if that too is negative consider therapeutic ^{131}I ablation

https://onlinelibrary.wiley.com/doi/pdf/10.1111/cen.12515

Question 40

A 75 year old presents with history of weight loss, palpitations and heat intolerance of 8 weeks duration. Examination reveals a resting tremor and atrial fibrillation with a ventricular rate of 110bpm. He is a haemodynamically stable and has a goitre on palpation of the neck. An ultrasound of the neck confirms the presence of multiple nodules in the thyroid gland with the largest of the nodules measuring 0.6 cm in size. His TFTs show suppressed TSH of < 0.01 and free T4 which is mildly elevated. What is the most appropriate modality which can be used for his definitive management?

- **A)** Carbimazole
- **B)** Observe
- **C)** Propylthiouracil
- **D)** Radioiodine ablation
- **E)** Total thyroidectomy

Answer

Correct answer : Radioiodine ablation

The patient has underlying toxic multinodular goitre which should be initially rendered euthyroid by using thioamide therapy (carbimazole or propylthiouracil). These are usually effective in controlling the hyperthyroid state but not curative. The treatment of choice in such patients remains radio-iodine ablative therapy. Surgical removal of the gland can be offered but would be regarded as second line to radio-iodine in this scenario.

Question 41

A 64 year old lady with known Hashimoto's thyroiditis presents with features of tiredness, cold intolerance and constipation. Apart from being on thyroxine 250 µg/ day, she is on ferrous fumarate tablets and takes alendronate 70 mg/ week.
On examination she has a pulse of 56bpm, cold extremities and delayed knee reflexes. Her biochemistry results are as shown below:

		Normal Ranges
Sodium	136 mmol/L	(135-145)
Potassium	4.1 mmol/L	(3.5-5.5)
Urea	6.2 mmol/L	(3-8)
Creatinine	84 µmol/L	(60-115)
FreeT^4	8.4 pmol/L	(11.5-22.7)
TSH	18.1 mU/L	(0.35-5.5)
Anti TPO antibody	Positive	
Haemoglobin	12.8 g/dL	(12-16)
Ferritin	302 pmol/L	(30-330)

What is the most appropriate course of action in her management for her overall improvement?

- **A)** Increase the thyroxine dose to 275 µg/ day
- **B)** Repeat the TFTs in 6 weeks
- **C)** Start her on vitamin C tablets
- **D)** Stop the alendronate tablets
- **E)** Stop the iron tablets

Answer

Correct answer : Stop the iron tablets

The following is a list of the major causes leading to persistently elevated TSH levels despite adequate thyroxine therapy:

- Compliance
- Drugs such as omeprazole, ferrous sulphate, calcium carbonate
- Malabsorption syndromes like coeliac disease
- Nephrotic syndrome

Compliance with the medications is the commonest cause for persistently elevated TSH levels despite adequate thyroxine replacement. In this lady normal ferritin and Hb levels indicate a trial without ferrous fumarate tablets which may help to prevent any interference with thyroxine absorption. Alternatively, thyroxine and iron tablets should be taken separately.

Question 42

A 24 year old with Type I diabetes mellitus and autoimmune thyroiditis, presents to the endocrine clinic with history of 6 kg of weight loss over the last 4-6 months. She denies going on any diet or indulging in excessive exercise. She denies any issues regarding compliance with insulin injections and/ or thyroxine tablets. Her appetite is normal and she denies any nausea and vomiting. Her bowel habits though have been irregular for 6 months. On examination she has a BMI of 21 kg/m^2 and general physical as well as systemic examination is unremarkable. Her blood results show:

		Normal Ranges
Haemoglobin	9.4 g/dL	(12-16)
Sodium	139 mmol/L	(135-145 mmol/L)
Potassium	4.4 mmol/L	(3.5-5.5 mmol/L)
Urea	5.3 mmol/L	(3-8 mg/dL)
Creatinine	66 µmol/L	(60-115 µmol/L)
FT^4	7.8 pmol/L	(11.5-22.7 pmol/L)
TSH	14.4 mU/L	(0.35-5.5 mU/L)
Anti TPO antibody	Positive	
Corrected Calcium	2.04 mmol/L	(2.2-2.6 mmol/L)

What is the most appropriate next step in her management?

- **A)** Anti TTG antibodies
- **B)** Assess urinary protein loss
- **C)** Check compliance
- **D)** Upper GI endoscopy
- **E)** 21 alpha hydroxylase

Answer

Correct answer : Anti TTG antibodies

The following is a list of the major causes leading to persistently elevated TSH levels despite adequate thyroxine therapy:

- Compliance
- Drugs such as omeprazole, ferrous sulphate, calcium carbonate
- Malabsorption syndromes like coeliac disease
- Nephrotic syndrome

In her case history of weight loss, alteration in bowel habit, low Hb and low corrected calcium should raise the suspicion of associated coeliac disease.

Question 43

Which of the following is suggestive of the suspicious nature of the radiology of a thyroid nodule?

- **A)** Colloid within the nodule
- **B)** Haemorrhage within the nodule
- **C)** Increased iodine uptake in the nodule
- **D)** Micro-calcification
- **E)** Presence of multiple nodules sub-centimetre nodules

Answer

Correct answer : Micro-calcification

Ultrasound features suggestive of thyroid malignancy:

>1cm sized nodule which is taller than it is wide

Microcalcification

Local invasion and lymph node metastases

Ill-defined and irregular margin and contour

Intrinsic hypervascularity

Solid and hypoechoic

Absence of a completely uniform halo around the nodule

US features suggestive of thyroid malignancy

According to the guidelines issued by the British Thyroid Association on management of thyroid cancer, the following are considered to be risk factors for thyroid cancer:

- History of neck irradiation in childhood
- Endemic goitre
- Hashimoto's thyroiditis (increased risk of lymphoma)
- Family or personal history of thyroid adenoma
- Cowden`s syndrome
- Familial adenomatous polyposis
- Familial thyroid cancer

A thyroid nodule is more likely to be malignant if:

- The affected individual is a child or an elderly male
- It is a firm, solitary, non toxic nodule
- Associated hoarseness of voice and/or palpable cervical lymph node
- In the presence of micro-calcification on fine-needle aspiration cytology

Question 44

A 32 year old lady with known papillary carcinoma of the thyroid (which was treated with total thyroidectomy and postoperative radio-iodine ablation 3 years ago), presents to the GP for a routine check up. Presently she is on thyroxine 75 µg/day and otherwise well in herself. Her examination is normal with evidence of a healed thyroid scar and no palpable cervical lymph nodes. Her biochemical results are as shown below:

		Normal Ranges
Sodium	136 mmol/L	(135-145)
Potassium	4.1 mmol/L	(3.5-5.5)
Urea	8 mmol/L	(3-8)
Creatinine	92 µmol/L	(60-115)
FT^4	14.8 pmol/L	(11.5-22.7)
TSH	2.2 mU/L	(0.35-5.5)
Anti TPO antibody	Negative	
Corrected Calcium	2.26 mmol/L	(2.2-2.6)

What is the most appropriate next step in her management?

- **A)** Arrange Ultrasound of the neck
- **B)** Check Calcitonin levels
- **C)** Decrease thyroxine dose
- **D)** Increase thyroxine dose
- **E)** Repeat TFTs in 4-6 weeks

Answer

Correct answer : Increase thyroxine dose

Really interesting case and a challenging management plan. Generally, this patient presents a low risk of recurrance but it seems that she has not had adequate thyroxine replacement in the past. Generally the aim in this patient would have been to titrate the thyroxine dose to keep TSH levels <0.01 mu/l. However, that doesn't seem to have happened here so the dose of thyroxine should be increased anyway by 25-50 mcg reflecting the increased metabolic demands.

https://www.hindawi.com/journals/jtr/2011/549609/

Question 45

A 32 year old lady is noticed by GP on routine examination to have a <1 cm thyroid nodule. She has no history of radiation exposure as a child and no family history of polyposis coli. She is otherwise well and the size of the nodule has not changed over the last 3-4 years. Her biochemistry reveals TFTs being within the normal range. What is the most appropriate next step in her management?

- **A)** Check Tg levels
- **B)** Early referral
- **C)** Manage in primary care
- **D)** Routine referral
- **E)** Urgent referral

Answer

Correct answer : Manage in primary care

The following table shows the summary of the British Thyroid Association (BTA) guidelines to the GP regarding referral of a thyroid nodule:

Same day	Urgent	Non Urgent	Managed by GP
Stridor associated with thyroid lump	Palpable cervical lymph nodes	Patient with hyper or hypothyroidism refer to endocrinologist	No change in size over years
	Rapidly enlarging (days-weeks)	Lump enlarging over months	No known risk factors
	Presence of risk factors for thyroid cancer	Sudden pain and enlarged mass (bleeding in a cyst)	<1cm, incidental thyroid nodule
	Hoarseness of voice		
	Nodule in a child		

Question 46

What is the likely physiological mechanism involved in critically unwell patients leading to a sick euthyroid state?

- **A)** Decrease in 3^1 deiodinase Type 1 levels
- **B)** decrease in 5^1 deiodinase Type 1 levels
- **C)** Increase in 5^1 deiodinase Type 3 levels
- **D)** Increase in 3^1 deiodinase Type 1 levels
- **E)** Increase in TBG levels

Answer

Correct answer : decrease in 51 deiodinase Type 1 levels

The conversion of T^4 to T^3 is mediated by the activity of 5^1 deiodinase enzymes. Deiodination of the outer ring of T^4 results in formation of T^3 (3-8 times more potent than T4), while deiodination of the inner ring leads to formation of reverse T^3 (metabolically inert). Three different types of 5^1 deiodinase are known to exist.

The following table shows a summary of different 5^1 deiodinase enzymes and their respective role:

Type	Location	Role	Significance
51 deiodinase Type 1	Most abundant of all, Present in liver, muscle and kidney etc	Acts on both outer as well as inner ring of thyroxine (T4)	Increases in hyperthyroid state and vice versa PTU inhibits it (not CBZ)
51 deiodinase Type 2	Neurons	Acts on outer ring to step up T3 production	Provide T3 to brain
51 deiodinase Type 3	Placenta foetal liver	Acts on inner ring to produce metabolically inert RT3	Protect placenta from excess T4 and T3

Question 47

What is the likely mechanism involved in thyroid hormone resistance?

- **A)** β chain mutation
- **B)** Mutation in glycoprotein receptor
- **C)** Nuclear receptor defect
- **D)** Thyroxine hormone synthesis defect
- **E)** Thyroxine hormone ultra-filtration defect

Answer

Correct answer : β chain mutation

Resistance to thyroid hormone can either be generalised, selective pituitary or selective peripheral resistance to hormone action. Most of the resistance syndromes are familial in origin. Patients are generally clinically euthyroid (except in cases of pituitary resistance to thyroid hormone) and the presence of goitre is sometimes the only positive sign. The mutation is usually at thyroid hormone receptor level. The β chain gene for the receptor is defective resulting in defective binding of thyroid hormones to the receptor. Most of the patients do not require any treatment. The biochemistry shows an elevated TSH level with normal or rarely high Free T^4 and Free T^3 levels. An important differential diagnosis in such a scenario is a TSHoma.

Question 48

What's the likely mode of action of carbimazole?

- **A)** Inhibition of the sodium - iodide symporter
- **B)** Inhibition of thyroid peroxidase activity
- **C)** Inhibition of conversion of T^4 to T^3
- **D)** Inhibition of TBG
- **E)** Inhibition of TSH receptors

Answer

Correct answer : Inhibition of thyroid peroxidase activity

Carbimazole (CBZ) and propylthiouracil (PTU) act by inhibiting the action of thyroid peroxidase (TPO) enzyme. PTU in addition inhibits the peripheral conversion of T_4 to T_3 (by inhibition of 5^1 deiodinase type 1 activity). Perchlorate and thiocyanates inhibit iodide transport.

Question 49

A 38 year old gentleman presents with a 3 month history of weight loss, palpitations and tremors. On examination he has a small goitre and fine tremors in both hands. His blood results are as shown below:

		Normal Ranges
Free T_4	28.2 pmol/L	(11.5-22.7 pmol/L)
Free T_3	8.1 pmol/L	(3.5-6.5 pmol/L)
TSH	5.2 mU/L	(0.35-5.5 mU/L)
AntiTPO	negative	
Anti TSH antibody	negative	

What's the next investigation to establish the diagnosis?

- **A)** A-subunit ratio
- **B)** MRI brain
- **C)** Thyroxine-binding globulin (TBG) levels
- **D)** Thyrotropin releasing hormone (TRH) stimulation test
- **E)** Thyroid stimulating hormone (TSH) receptor antibodies

Answer

Correct answer : A-subunit ratio

The presence of inappropriately normal or elevated TSH levels in the presence of elevated T_3 and T_4 levels is indicative of either a TSH secreting pituitary adenoma or thyroid hormone resistance. Rarely such a biochemical profile is a result of the presence of heterophile antibodies leading to spurious results. TSH secreting tumours usually present with features of mild thyrotoxicosis and goitre. The TSH a-subunit secretion is increased in such tumours and is used to distinguish from thyroid hormone resistance. A molar ratio of a-subunit to TSH of > 5.7 is considered diagnostic in such cases. A TRH stimulation test can occasionally be used to distinguish between the two conditions but is hardly performed these days.

In contrast thyroid hormone resistance can either be generalised, selective pituitary or selective peripheral (resistance to hormone action). Most of the resistance syndromes are familial in origin. Patients are generally clinically euthyroid except in cases of pituitary resistance to thyroid hormone. The mutation is usually at thyroid hormone receptor level.

Question 50

A 32 year old woman has decided to go on a strict vegan diet for a year. She has recently returned from a world tour and visited sub-Saharan countries and went on an expedition in the Himalayas. She presents with a diffuse smooth goitre. Her bloods show a euthyroid status and negative anti TPO antibodies. What is the next investigation to establish the likely diagnosis?

- **A)** CT neck
- **B)** Fine-needle aspiration cytology (FNAC)
- **C)** US neck
- **D)** Urinary iodide excretion
- **E)** Uptake scan

Answer

Correct answer : Urinary iodide excretion

Enlargement of the thyroid gland (goitre) can be secondary to physiological states of increased iodide demand such as puberty and pregnancy, congenital defects of thyroid hormone synthesis, iodide deficiency, autoimmune thyroiditis (Hashimoto's thyroiditis), drug induced (amiodarone, lithium, interferon), postpartum thyroiditis etc.

In the developed world iodine deficiency goitre is uncommon as the optimum iodide requirement of 150 µg per day (according to WHO recommendations) is easily met through diet. This patient has been on a world tour and visited iodide depleted areas such as the Himalayas making her susceptible to iodine deficiency goitre. As more than 95% of dietary iodide is excreted in urine, a 24 hour urinary excretion of iodide is an excellent index of dietary iodine intake and can unmask an iodide deficiency state.

Question 51

A 42 year old lady presents to clinic complaining of a lump in her neck. In her past medical history she has been treated for left breast cancer requiring surgery, 6 years ago and has been in remission since.

On examination, she is noted to have some small nodules on her tongue. There is a 1.2 cm, firm, left sided thyroid nodule. There is no palpable cervical lymph nodes. Which of the following is the likely underlying diagnosis?

- **A)** Carney complex
- **B)** Cowden syndrome
- **C)** MEN 2b syndrome
- **D)** Neurofibromatosis
- **E)** vHL syndrome

Answer

Correct answer : Cowden syndrome

Cowden syndrome is an Autosomal dominant condition a consequence of an inactivating mutation of PTEN tumour suppressor gene. It is characterised by multiple hamartomas involving all the germ cell layers, susceptibility to develop breast, thyroid and endometrial cancers and involvement of the thyroid gland in the majority of patients. The thyroid pathologies associated with Cowden syndrome include differentiated thyroid carcinomas, adenomas and multinodular goitre.

https://emedicine.medscape.com/article/1093383-overview

Question 52

A 75 year old gentleman presents to the endocrine clinic with an 8 week history of weight loss, palpitations and tremors. He has past medical history of ischaemic heart disease and atrial fibrillation (AF). He is currently taking aspirin, ramipril, metoprolol and rosuvastatin. He was on amiodarone which was stopped recently by the cardiologist (1 week ago). His blood results are as shown below:

		Normal Ranges
TSH	< 0.01mU/L	(0.35-5.5 mU/L)
Free T_4	28 pmol/L	(11.5-22.7 pmol/L)
Free T_3	7.9 nmol/L	(3.5-6.5 pmol/L)
Anti TPO	negative	
Uptake scan	< 1% uptake	

What is the most appropriate next therapeutic option for his management?

- **A)** Carbimazole
- **B)** Prednisolone
- **C)** Propylthiouracil
- **D)** Propranolol
- **E)** Radioiodine ablation

Answer

Correct answer : Prednisolone

Amiodarone has a close structural resemblance to thyroxine and contains 2 atoms of iodine per molecule which represent approximately 37.5% of its molecular weight. It has a wide tissue distribution and a half life of 52.6 days. Abnormalities of the thyroid gland are extremely common in patients on amiodarone and include both hypothyroidism (AIH) as well as thyrotoxicosis (AIT).

AIT in turn can be secondary to iodide excess (AIT -Type 1) usually on the background of an abnormal thyroid gland or due to an inflammatory reaction evoked by amiodarone (AIT - Type 2). The clinical distinction between these two types is often extremely difficult. AIT-Type 2 is generally associated with no signs of clinical thyroid disease, negative thyroid autoantibody status and decreased uptake on radioiodine scan.

Discontinuation of amiodarone therapy (if possible) and steroids form the mainstay for treatment of AIT - Type 2. While in AIT -Type 1, thioamides (CBZ, PTU) are generally effective. Due to practical difficulties to distinguish between the 2 types, often a combination of steroids and thioamides is used for treatment of AIT.

Question 53

A 74 year old with a past medical history of life threatening arrhythmias, is on long term amiodarone therapy and was fitted with a defibrillator 2 years ago. He has been clinically asymptomatic for the last year as far as symptoms of palpitations are concerned. His recent routine blood tests show:

		Normal Ranges
TSH	15.5 mU/L	(0.35-5.5 mU/L)
Free T_4	4.6 pmol/L	(11.5-22.7 pmol/L)
Anti TPO	negative	

What is the next therapeutic intervention you will consider?

- **A)** Liothyronine 20 µg twice a day
- **B)** Radioiodine ablation
- **C)** Start thyroxine 25 µg per day
- **D)** Start thyroxine 50 µg per day
- **E)** Stop amiodarone

Answer

Correct answer : Start thyroxine 25 µg per day

This patient has amiodarone-induced hypothyroidism which is the commonest side effect associated with amiodarone treatment in iodine replete areas (in contrast to amiodarone induced thyrotoxicosis more commonly seen in iodine depleted areas). Discontinuation of amiodarone should be considered if possible. In this case because of a previous history of life threatening arrhythmias the safer option would be to start with a low dose of thyroxine.

Question 54

A 31 year old woman who is 11 weeks pregnant presents with tachycardia, tremors and palpitations. She has a strong family history of autoimmune thyroid disease and goitre. Her thyroid function test results are as shown below:

		Normal Ranges
Free T_4	32.8 pmol/L	(9-23)
Free T_3	11.2 pmol/L	(3.5-6.5)
TSH	< 0.01 mU/L	(0.35-5.5)

What is the best therapeutic option in her case?

- **A)** Carbimazole
- **B)** Lugols iodine
- **C)** Propranolol
- **D)** Propylthiouracil
- **E)** Radioiodine

Answer

Correct answer : Propylthiouracil

The patient is likely to have Graves' thyrotoxicosis as suggested by features of hyperthyroidism and an associated strong family history of autoimmune thyroid disease. In view of her pregnant state, treatment with lowest dose of propylthiouracil, which renders her euthyroid, should be initiated. The following are a few salient points to be remembered as far as pregnancy and thyroid dysfunction is concerned:

- Thyroxine requirements increase in hypothyroid women during the first trimester of pregnancy.
- TSH levels increase during the 2^{nd} and 3^{rd} trimesters of pregnancy.
- Hyperthyroidism in pregnancy is commonly due to Graves' disease (d/d hyperemesis gravidarum, H mole), so check TSH receptor antibodies (TRAb) in all such patients.
- Graves' disease can relapse during first trimester and postpartum period (more likely to remit during 2^{nd} and 3^{rd} trimester)
- Check TRAb in the third trimester, as it can be transmitted through the placenta to the baby, leading to neonatal hyperthyroidism
- Treat maternal hyperthyroidism with the lowest possible dose of PTU (more protein bound, less transfer across placenta)
- 1 out of 4 type 1 diabetics, have evidence of thyroid dysfunction during pregnancy

Question 55

A 35-year-old lady presents with a 1.5 cm nodule in her thyroid. Ultrasound thyroid scan did not show features of malignancy. Fine-needle aspiration cytology (FNAC) results show THY2 lesion. What should be the most appropriate step in her management?

- **A)** Lobectomy
- **B)** Reassure and discharge
- **C)** Radioiodine ablation
- **D)** Refer for total thyroidectomy
- **E)** Repeat FNAC in 3-6 months

Answer

Correct answer : Reassure and discharge

The guidelines from the British Thyroid Association (BTA) recommend no further investigations if Ultrasound thyroid did not show any evidence of malignancy.

Question 56

A 45 year old with a 1 cm nodule in the thyroid, undergoes a fine-needle aspiration cytology (FNAC). The results of FNAC show THY3a. What is the next step in management?

- **A)** Lobectomy
- **B)** Reassure and discharge
- **C)** Radioiodine ablation
- **D)** Repeat FNAC
- **E)** Total thyroidectomy

Answer

Correct answer : Repeat FNAC

Thy3 means neoplasm possible. This is again divided into: Thy3a and Thy3f Thy3a – when there are atypical features present but not enough to place into any of the other categories. The cytological interpretation should be clearly stated in the report and may include situations such as inability to exclude a follicular cancer or papillary carcinoma. Many Thy3a cases reflect suboptimal specimens and can be re-allocated on repeat cytology. Thy3f – when a follicular neoplasm is suspected. The histological possibilities then include a hyperplastic nodule, follicular adenoma or follicular carcinoma. These cannot be distinguished on cytology alone and a histology sam- ple (e.g. diagnostic hemithyroidectomy) will be required for diagnosis. Follicular variant of papillary thyroid carci- noma will also sometimes fall into this category when the nuclear features are more subtle Reference: The British Thyroid Association Guidelines for the Management of Thyroid Cancer 2014

Question 57

A 60 year old woman is admitted with a history of being acutely unwell, with diarrhoea and more recent confusion. She gives no other history of note and is particularly agitated on admission. Her husband informs you that she has little of note in her history but has become increasingly agitated and has lost weight over the last one month.

Examination reveals that she is confused with a Glasgow coma score of 15. She has a BMI of 18 kg/m2, a pulse of 120 bpm irregular, blood pressure of 110/65 mmHg and a temperature of 38.9^{O}C. She has an obvious goitre with an audible bruit.

Results reveal:

FBC	Normal
U+Es	Normal
CRP	15 (<5)
ECG	Atrial fibrillation

Which of the following is the most appropriate initial treatment for this patient?

- **A)** IV amoxicillin and metronidazole
- **B)** IV potassium Iodide
- **C)** IV propranolol
- **D)** Oral carbimazole
- **E)** Oral propylthiouracil

Answer

Correct answer : IV propranolol

This patient appears to be developing thyroid storm as revealed by a temperature, agitation, confusion, atrial fibrillation and goitre. We are not provided with the TFTs as these will often take some time to process even if asked for acutely. In this case the IV beta-blockers would be the most appropriate approach as treatment for the atrial fibrillation and these also prevent the peripheral conversion of T4 to T3. Either oral propylthiouracil or carbimazole should be given but both will take 2 hours to have an effect on the production of thyroid hormone and of course neither will prevent the release of stored hormone. Thioamides must be given at least one hour prior to the use of iodides which do block the release of stored hormone. Also, the patient should receive IV steroids.

Reference:

- Forth Valley Guidelines on thyroid storm

Question 58

What is the daily Iodine requirement for a healthy adult as per the WHO recommendations?

- **A)** 10 micrograms
- **B)** 150 micrograms
- **C)** 500 micrograms
- **D)** 1 mg
- **E)** 3mg

Answer

Correct answer : 150 micrograms

Explanation:

The daily Iodine requirements recommended by the WHO:

Age	Iodine requirement
0 to 11 months	50 microgram
12 to 59 months	90 microgram
6 to 12 years	120 microgram
>12 and adults	150 microgram
Pregnant and lactating women	200 microgram

Question 59

A 37-year-old woman attended the thyroid clinic. She had a past medical history of Graves' disease for which she was treated with a 12-month course of carbimazole. Two years after treatment she had a relapse of the thyrotoxicosis. She did not have Graves' ophthalmopathy and was a non-smoker. She did not have any children. Radioactive iodine therapy (RAI) was considered and all the safety precautions were explained to her. She was enquiring about the chances of her becoming hypothyroid with the RAI therapy.

What is the prevalence of hypothyroidism at 10 years following RAI therapy?

- **A)** 10 %
- **B)** 30 %
- **C)** 40%
- **D)** 50%
- **E)** 70 %

Answer

Correct answer : 50%

Explanation:

The prevalence of hypothyroidism is about 50% at 10 years post RAI therapy. Initially, it may be transient. TSH should be monitored initially, then annually after radioiodine to determine late hypothyroidism. The incidence of hypothyroidism is lower with autonomous toxic nodule since the nodule takes up the radioactive iodine while the surrounding tissue will recover normal function.

https://www.google.com/
url?sa=t&rct=j&q=&esrc=s&source=web&cd=2&cad=rja&uact=8&ved=2ahUKEwi5idGd4MfmAhUiQEEAH
CAcQFjABegQIARAC&url=http%3A%2F%2Fwww.thyroiduk.org.uk%2Ftuk%2Fguidelines%2FRadioiodine
qB3L8Zvl_xHm-DQZP

Question 60

A 78-year-old man had attended the thyroid clinic. He had a 20-year history of a slowly progressive goitre. Until recently his goitre had not caused any problems. For the last few months he was complaining of difficulty breathing and a sensation of choking. He had a past medical history of severe heart failure and ischaemic heart disease. Clinically he was euthyroid and he had a medium sized goitre (90 ml). He did not have any clinical signs of Graves' disease. His thyroid function tests have come back as normal. He was diagnosed with an euthyroid goitre. An ultrasound thyroid scan excluded a malignancy. He was a high risk for surgery and therefore he was considered for radioactive iodine therapy (RAI) to reduce the size of his goitre.

What percentage reduction in goitre is expected in this patient following RAI therapy?

- **A)** No reduction
- **B)** 10 %
- **C)** 30 %
- **D)** 50 %
- **E)** 80 %

Answer

Correct answer : 50 %

Explanation:

Radioiodine is being increasingly used for the management of euthyroid goitre once malignancy has been excluded. If the goitre is causing significant cosmetic complaints or symptoms or signs of obstruction of the upper airways or oesophagus, surgery is considered the treatment of choice, but radioiodine should be discussed as an alternative treatment, especially in those patients with significant co-morbidity in whom surgery may be high risk. In those with small to medium sized goitres (<100 ml in volume) there is an approximate 50% reduction in goitre size following radioiodine treatment, half of the effect being evident within the first three months.

Reference:

- Clinical guidelines, 2007, Radioiodine in the management of benign thyroid disease: Report of a Working Party. London, Royal College of Physicians (RCP)

Question 61

A 45-year-old woman was referred by the GP to thyroid clinic for a lump in her neck, which was noticed about 2 weeks ago by her husband. She denied neck pain, weight loss or hoarseness of voice. She did not have any past medical history. She was a smoker of 10 cigarettes per day. She occasionally drinks alcohol. She does not take any regular medications. On examination there was a 3x2 cm left sided thyroid nodule and there was no palpable cervical lymphadenopathy. Her systemic examination was unremarkable. Later she underwent an ultrasound scan of the thyroid as per the guidelines.

Which of the following characteristics on thyroid ultrasound is more predictive of malignancy?

- **A)** Central vascularity
- **B)** Hypo echogenicity
- **C)** Incomplete halo
- **D)** Irregular margins
- **E)** Micro calcifications

Answer

Correct answer : Micro calcifications

Explanation:

All the above features are seen in malignancy. However, intra nodular micro calcifications favor the diagnosis of malignancy. Micro calcifications less than 2mm in diameter were observed in 60% of malignant thyroid nodules but in less than 2% of benign thyroid nodules.

Question 62

The thyroid hormone synthesis is inhibited by a variety of agents. These agents are called goitrogens. What is the mechanism of action of perchlorate?

- **A)** Inhibition of coupling of iodothyronines
- **B)** Inhibition of initial oxidation of Iodide
- **C)** Inhibition of intrathyroidal iodine metabolism
- **D)** Inhibition of iodide transport
- **E)** Inhibition of thyroid peroxidase

Answer

Correct answer : Inhibition of iodide transport

Explanation:

Various agents inhibit thyroid hormone synthesis. Perchlorate and thiocyanate inhibit iodide transport. Thionamides inhibit initial oxidation of iodide and coupling of iodothyronines

Question 63

A 30-year-old pregnant woman has attended the antenatal clinic. She is currently 10 weeks pregnant and this is her second pregnancy. She has a past medical history of asthma, which is well controlled. She takes inhalers for asthma. Her thyroid peroxidase (TPO) antibodies during early gestation were strongly positive. What is the chance of her developing hypothyroidism in the post-partum period?

- **A)** 1%
- **B)** 5%
- **C)** 20%
- **D)** 50%
- **E)** 90%

Answer

Correct answer : 50%

Explanation:

The measurement of thyroid antibodies (thyroid peroxidase, TPO and TSH receptor) does not give any indication of thyroid functional status. The presence of these antibodies will have adverse implications on pregnancy. TPO antibodies are a marker for an increased risk of infertility, miscarriage and preterm delivery. TPO antibodies are found in approximately 10% of women in early pregnancy and development of hypothyroidism is also possible during pregnancy. The finding of TPO antibodies in early pregnancy imparts a 50% risk for the development of postpartum thyroid dysfunction and the postpartum thyroiditis.

References:

- John H. Lazarus; Thyroid function in pregnancy, British Medical Bulletin, Volume 97, Issue 1, 1 March 2011, Pages 137-148

Question 64

A 56-year-old woman was referred to thyroid clinic for abnormal thyroid functional tests. She was completely asymptomatic related to her thyroid dysfunction. About a month ago she had non-specific abdominal pain for which she had a contrast-enhanced CT scan of the abdomen. Previous TFTs had been normal. She does not take any regular medication. On examination, she appeared well with no features of thyroid dysfunction. Her systemic examination was unremarkable.

Her thyroid function tests are as follows

		Normal Ranges
TSH	0.01 mU/L	(0.35-4.5)
Free T4	20.6 pmol/L	(11.5-19.7)
Free T3	6.2pmol/L	(3.5-6.5)

Thyroid receptor antibodies were negative.

What is the most likely underlying diagnosis in this case?

- **A)** De Quervain’s thyroiditis
- **B)** Graves’ disease
- **C)** Iodine induced thyroid dysfunction
- **D)** Solitary toxic nodule
- **E)** Thyroid hormone resistance

Answer

Correct answer : Iodine induced thyroid dysfunction

Explanation:

The likely cause of thyroid dysfunction in this patient is iodine-induced hyperthyroidism. In most cases, contrast-induced thyroid dysfunction is transient. Patients with renal failure, underlying thyroid disease, or a history of thyroid dysfunction are also at higher risk of contrast-induced thyroid dysfunction. These patients should be closely monitored for thyroid dysfunction after receiving iodine contrast medium.

Question 65

A 65-year-old lady presented with a 6-month history of palpitations, sweating and weight loss. She had a history of multinodular goitre, which was treated with radioactive iodine therapy about a year ago. Clinically she was in a sinus rhythm with a heart rate of 110/min. She had moderate sized goitre. She did not have any eye signs. Her systemic examination was unremarkable.
Her thyroid function tests were as follows:

		Normal Ranges
TSH	0.01 mU/L	(0.35-4.5)
Free T4	30.8 pmol/L	(11.5-19.7)
Free T3	7.2pmol/L	(3.5-6.5)

Her thyroid receptor antibodies were negative. The underlying diagnosis was likely due to recurrence of multinodular goitre. What is the most appropriate definitive management in this patient?

- **A)** Carbimazole for 1 year
- **B)** Lithium
- **C)** Propylthiouracil for a year
- **D)** Second dose of radioactive therapy
- **E)** Total thyroidectomy

Answer

Correct answer : Second dose of radioactive therapy

Explanation:

In this patient the first dose of RAI had been ineffective. The next best step is a further dose of RAI provided if it is after 6 months of the first RAI therapy.

Question 66

You see a 45 year old teacher with papillary thyroid cancer, a rising thyroglobulin and known lung metastases. Which of the following is the most appropriate treatment for this patient?

- **A)** 5 Fluoro-Uracil
- **B)** Ablative I-131
- **C)** Arimidex
- **D)** I -131 MIBG (metaiodobenzylguanidine)
- **E)** Somatostatin analogue

Answer

Correct answer : Ablative I-131

The majority of patients with a tumour more than 1 cm in diameter, who have undergone a near-total/total thyroidectomy, should have 131I ablation (section 5.2)
(British thyroid association Thyroid cancer guidelines 2007).

Question 67

A 45-year-old man presented to the thyroid clinic with a complaint of a lump in the neck that was first noticed about 3 weeks ago. There was no significant past medical history. On examination he was afebrile, his pulse rate was 90 /min and blood pressure was 130/80mmHg. Examination of the neck revealed a 2 cm nodule palpable in the left lobe of the thyroid. Ultrasound assessment of the thyroid showed solid, hypoechoic nodules with globular calcification and intranodular vascularity.

These ultrasound features correlate with which grade of British Thyroid Association (BTA) Ultrasound (U) classification of thyroid nodules?

- **A)** U1
- **B)** U2
- **C)** U3
- **D)** U4
- **E)** U5

Answer

Correct answer : U5

Explanation:

The risk of thyroid cancer increases with age, particularly after the age of 40 years. Male gender has been reported as an independent risk factor in some studies. The size of the thyroid nodule correlates poorly with the risk of malignancy. Ultrasound is extremely sensitive and can be specific for the diagnosis of thyroid carcinoma (particularly papillary cancer). According to British thyroid association (BTA) guidelines, the use of the U1-U5 scoring/grading system is recommended for assessing the risk of malignancy and guiding FNAC.

This patient has a solid, hypoechoic nodule with globular calcification and intranodular vascularity on ultrasound. These features are suggestive of malignant nodule (U5). Cystic, isoechoic/mildly hyperechoic with peripheral eggshell calcification and peripheral vascularity is suggestive of benign nodule (U2). Solid, hypoechoic with mixed/central vascularity are features of indeterminate nodules (U3) while solid, hypoechoic with disrupted peripheral calcification are features of suspicious nodules (U4). Sonographically U1-U2 should be regarded as reassuring not requiring FNAC unless the patient has a high risk of malignancy, whereas for U3-U5, a US-guided FNAC should be performed.

Reference:

- Perros P. et. al. (2014) ‘British Thyroid Association Guidelines for the Management of Thyroid Cancer', Clinical Endocrinology 81(s1) 1-122. Wiley Online Library [Online]

Question 68

A 26-year-old lady presented to the thyroid clinic with a painless lump in her neck. She noticed it about 2 months ago. On examination, a 1.5 cm nodule was palpable in the right lobe of the thyroid. An ultrasound of the thyroid was performed and features were suggestive of U4 grade as per BTA Ultrasound (U) classification of thyroid nodules. She underwent FNAC and the histopathology report confirmed Thy 2 cytology.
What is the most appropriate management approach based on BTA guidelines?

- **A)** Discuss in thyroid MDT (multidisciplinary team) meeting
- **B)** Radioiodine ablation
- **C)** Reassure and discharge from further follow up
- **D)** Repeat FNAC
- **E)** Right lobectomy

Answer

Correct answer : Repeat FNAC

Explanation:

Patients with a history of a thyroid nodule or a thyroid nodule found on examination should be further assessed with ultrasound (US). The US is extremely sensitive and can be specific for the diagnosis of thyroid cancer. According to BTA guidelines, Ultrasound (U) classification of thyroid nodule (U1-U5 scoring/grading system) is recommended for assessing the risk of malignancy and guiding FNAC. Characteristic US features allow the differentiation of nodules as either normal (U1), benign (U2), indeterminate (U3), suspicion (U4) or malignant (U5). For U1-U2 features no FNAC is required unless the patient is at high risk of malignancy whereas, for U3-U5, US-guided FNAC should be performed.

Thy numerical diagnostic categories are used in BTA guidelines to interpret FNAC results as Thy 1 (non-diagnostic), Thy 2 (non-neoplastic), Thy 3 (neoplasm possible), Thy 4 (suspicious of malignancy) and Thy 5 (Diagnostic of Malignancy).

Follow up should depend on US appearance and associated cytology. This patient has Thy 2 cytology but suspicious US features (U4). According to BTA guidelines, such patients should undergo repeat FNAC for confirmation. The rate of malignancy in this setting is significant and evidence supports repeat cytological sample.

Reference:

- Perros P. et. al. (2014) ‘British Thyroid Association Guidelines for the Management of Thyroid Cancer', Clinical Endocrinology 81(s1) 1-122. Wiley Online Library [Online]

Question 69

A 38-year-old lady presented to the endocrine clinic for review. She had a history of Graves' disease for which she took carbimazole for 18 months. Her treatment was stopped as she was clinically and biochemically euthyroid. What is the rate of remission at 5 years after discontinuing therapy?

- **A)** 30%
- **B)** 40%
- **C)** 50%
- **D)** 60%
- **E)** 80%

Answer

Correct answer : 40%

Explanation:

Two different treatment regimens are practised for Graves' disease, dose titration and block and replace. In the dose titration regimen, patients are treated with a relatively high dose of carbimazole or propylthiouracil and then euthyroidism is maintained with a low stable dose. Free T4 (FT4) is monitored every 4-8 weeks aiming for FT4 in a normal range. The typical starting dose of carbimazole is 20-30 mg/day. Higher doses (40-60mg) may be indicated in severe cases with very high levels of FT4. Treatment is continued for 18 months. The remission rate is up to 40% at 5 years after discontinuing therapy. In the block and replace regimen, carbimazole 40 mg daily with thyroxine at 100 ug can be prescribed for 6 months. Relapses are most likely to occur within the first year in both regimens.

Reference:

- Wass, J. and Owen, K. (2014) Oxford handbook of Endocrinology and Diabetes. 3rd edn. Pakistan: Oxford University Press

Question 70

A 40-year-old lady was seen in an endocrine clinic for review. She had been diagnosed with hypothyroidism 5 years ago. She was taking a stable dose of thyroxine 150ug for the last 3 years with good compliance. She started on tamoxifen therapy 20 mg/day 3 months ago because of suspicious findings on her mammogram. She was clinically euthyroid and had a small firm thyroid without palpable nodules. Her complete blood count and LFTs were normal. Her thyroid function test showed:

Thyroid stimulating hormone (TSH)	8.5 mU/L	(0.35-5.5)
Free Thyroxine (FT4)	10.6 pmol/L	(11.5-22.7)

What is the most likely cause of this patient's raised TSH?

- **A)** Decreased absorption of thyroxine
- **B)** Decreased T4 synthesis
- **C)** Elevated levels of thyroxine binding globulin
- **D)** Impaired conversion of T4 to triiodothyronine (T3)
- **E)** Increased clearance of thyroxine

Answer

Correct answer : Elevated levels of thyroxine binding globulin

Explanation:

Over 99% of circulating T4 and T3 is protein-bound, with thyroxine-binding globulin (TBG) is the major binding protein. Oestrogens (including oral contraceptive) and selective oestrogen receptors (tamoxifen) can increase TBG which results in a parallel increase in serum levels of the total but not free T4 and T3 in normal persons. In persons unable to compensate for these increases such as in hypothyroidism, the dose of thyroxine needs to be increased. Other drugs that increase TBG level include methadone, heroin and 5-fluorouracil. So monitoring with thyroid function is required 8-12 weeks after starting these medications in hypothyroidism. Medications that impair thyroxine absorption include cholestyramine, colestipol, calcium carbonate, iron sulphate and drugs that inhibit gastric acid secretion. Tamoxifen doesn't decrease the absorption of thyroxine. Amiodarone, propranolol, propylthiouracil and glucocorticoids impair conversion of T4 to T3. Phenytoin, carbamazepine, phenobarbital and rifampin increase the clearance of T4. The use of these drugs in hypothyroidism may require an increase in the dose of thyroxine to maintain euthyroid state. Li, thionamides, thiocyanate, perchlorate and amiodarone decrease T4 synthesis. Tamoxifen doesn't impair T4 to T3 conversion or clearance of T4 or decrease T4 synthesis.

Reference:

- Arafah BM. (2001)' Increased need for thyroxine in women with hypothyroidism during estrogen therapy', N Engl J Med 344(23):1743-9.
- Wass, J. and Owen, K. (2014) Oxford handbook of Endocrinology and Diabetes. 3rd edn. Pakistan: Oxford University Press